



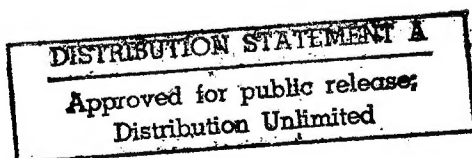
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# ***JPRS Report***

# **Science & Technology**

***Central Eurasia:  
Life Sciences***

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# Science & Technology

## Central Eurasia: Life Sciences

JPRS-ULS-92-011

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09 APRIL 1992

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**Hypoxic Stress Proteins From Human  
Lymphocytes Induced by  $\text{Ca}^{2+}$  Ions**

927C0247D Moscow DOKLADY AKADEMII NAUK  
SSSR in Russian Vol 321 No 1, Nov 91 (manuscript  
received 27 Aug 91) pp 210-213

[Article by A. A. Aldashev, K. A. Agibetov, A. A. Yugay,  
A. T. Shamshiyev, and Ye. V. Kim, Kyrgyz Cardiology  
Scientific Research Institute, Bishkek; UDC  
576.8.078.2:547.96:616-001.8]

[Abstract] Peripheral blood lymphocytes from male  
donors were used to test the effect of  $\text{Ca}^{2+}$  levels on  
hypoxins [as published]. It was shown that increasing the  
 $\text{Ca}^{2+}$  concentration in the medium to 25-50 mM elicited  
even stronger induction of Hyp38 than did hypoxia. In  
contrast, EGTA (2 mM) added to the medium sup-  
pressed the induction of Hyp38, thus suggesting that the

expression of hypoxin Hyp38 is regulated by the concen-  
tration of intracellular  $\text{Ca}^{2+}$ . The authors also demon-  
strated that the intracellular  $\text{Ca}^{2+}$  level increases in the  
first minutes after the onset of hypoxia. The expression  
of hypoxins increases 48 hours after hypoxia, indicating  
that hypoxins are stress proteins that regulate either  $\text{Ca}^{2+}$   
homeostasis in the cell or cellular phosphoinositide  
metabolism associated with it. These findings suggest  
that hypoxins may be either regulatory proteins that  
decrease the concentration of free  $\text{Ca}^{2+}$  inside the cell or  
enzymes that degrade inositol-1,4,5-triphosphate. These  
data demonstrate that the expression of Hyp38 is regu-  
lated by the concentration of intracellular  $\text{Ca}^{2+}$ . In  
conclusion, the results demonstrate that hypoxic stress  
proteins Hyp38 and Hyp52 are isoforms of inositol-  
1,4,5-triphosphate 3-kinase and that an increase in  $\text{Ca}^{2+}$   
is the main stress factor acting in the cell under condi-  
tions of hypoxia. Figures 2; references 15: 1 Russian, 14  
Western.



### Growth Kinetics and Light Production by Recombinant *Escherichia Coli* (Lum)

927C0300A Moscow BIOTEKHNOLOGIYA in Russian  
No 6, Nov-Dec 91 (manuscript received 17 Apr 91)  
pp 12-15

[Article by N. S. Markevichev, Ye. G. Melnichenko\*, L. Yu. Berzhanskaya\*, Yu. S. Krivoshein\*, and M. N. Manakov, Moscow Institute of Chemical Technology imeni D.I. Mendeleev; \*Crimean Medical Institute, Simferopol; UDC 57.083.13:591.557.61]

[Abstract] An analysis was conducted on the growth and nutritional factors affecting expression of luciferase in recombinant *E. coli* (lum). The *E. coli* strain was engineered by plasmid transmission of luciferase-encoding gene from *Photobacterium leiognathi*. Monitoring growth and light production parameters demonstrated that maximum luciferase expression occurred in the retardation phase of growth. Batch culture studies using various nutrient conditions provided support for the contention that light production requires reducing equivalents derived from assimilation of high MW nutrients. Figures 7; references 8: 5 Russian, 3 Western.

### Furaldehyde Biotransformation by *Candida Tropicalis*

927C0300B Moscow BIOTEKHNOLOGIYA in Russian  
No 6, Nov-Dec 91 (manuscript received 01 Oct 90)  
pp 16-18

[Article by A. I. Sizov, M. S. Frid, I. I. Balashevich, A. Ye. Ukhnaev and I. G. Shtepenko, 'Gidrolizprom' Scientific Industrial Association, Leningrad; UDC 582.282.23]

[Abstract] Kinetic studies were conducted on the transformation of furaldehyde to 2-furoic acid, an important industrial intermediate, by *Candida tropicalis* in order to assess the efficiency of this process and determine optimum synthetic conditions. The results showed that the rate limiting step in the transformation sequence furaldehyde > furfuryl alcohol > 2-furoic acid was the oxidation of the alcohol to the acid. Optimum conditions for biotransformation consisted of pH 6 and 38°C and a biomass concentration of 12 g/L (dry). In continuous cultures 2-furoic acid accumulation should be limited to 6.0 mM to preclude inhibition of the culture. Figures 5; references 15: 14 Russian, 1 Western.

### Use of *Agrobacterium Tumefaciens* Shooty Mutant for Enhancement of Regenerative Potential of Potato Explants In Vitro

927C0300C Moscow BIOTEKHNOLOGIYA in Russian  
No 6, Nov-Dec 91 (manuscript received 04 Jul 91)  
pp 19-22

[Article by V. A. Avetisov, A. M. Stefanovich, Yu. V. Davydova and O. S. Melik-Sarkisov, All-Union Scientific

Research Institute of Agricultural Biotechnology, All-Union Academy of Agricultural Sciences, Moscow; UDC 581.143]

[Abstract] *Solanum* plants were employed in a study on the effects of an increase in the endogenous cytokinin pool on plant development. The study involved leaf explants of several potato (*Solanum tuberosum*) varieties and a wild type (*S. vernei*) infected with *Agrobacterium tumefaciens* pGV 2206 (shooty mutant) bearing a cytokinin gene. Subsequent cultivation of the potato explants on Murashige and Skoog medium demonstrated that infection increased the incidence of callus formation and accelerated its rate of development. Cultivation on media supplemented with 6-benzylaminopurine had no telling effect on the formation and development of the calluses. Uninfected and infected wild-type potato explants failed to form runners on hormone-free medium. Following culture on hormone-enriched medium only infected wild-type *solanum* formed runners. These observations indicate that *A. tumefaciens* pGV 2206 may be used for engineering novel plant varieties with enhanced potential for in vitro development. Figures 1; tables 3; references 11: 1 Romanian, 5 Russian, 5 Western.

### N-Acetylglucosaminyl-N-Acetylmuramyl-L-Alanyl-D-Isoglutamine Adjuvant for In Vitro Immunization in Production of Monoclonal Antibodies Against IL-1 B (163-171) Peptide

927C0300D Moscow BIOTEKHNOLOGIYA in Russian  
No 6, Nov-Dec 91 (manuscript received 07 Aug 91)  
pp 23-25

[Article by S. V. Guryanova, T. M. Andronova and N. G. Safonova, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow; UDC 612.112.94:017.1.086.83]

[Abstract] N-Acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine, a glycopeptide fragment of bacterial cell walls, was tested for efficacy as an adjuvant for in vitro generation of monoclonal antibodies against the IL-1  $\beta$  (163-171) peptide. The essential approach involved incubation of 10E6/ml of splenic cells from two month old BALB/c female mice with 10  $\mu$ g/ml of the adjuvant and 0.05  $\mu$ g/ml of the antigen coupled to KHL for four days in RPMI 1640 medium with 20 percent FBS in CO<sub>2</sub> incubator. Following fusion with X-63 Ag 8,653 myeloma cells and cloning, ELISA demonstrated that 17 percent of the clones produced monoclonal antibodies. The efficacy of N-Acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine as an adjuvant in in vitro immunization opens new vistas in generating monoclonal antibodies in a considerably shorter period of time than by conventional in vivo methods. Tables 1; references 19: 6 Russian, 13 Western.



**Serum-Free Media for Mammalian Cells. Part V.  
Culture of HIV-1 Producing Lymphocytes in  
Embryonal Serum-Free Media**

927C0300E Moscow BIOTEKHNOLOGIYA in Russian  
No 6, Nov-Dec 91 (manuscript received 29 Oct 90)  
pp 64-66

[Article by A. I. Koreneva\*, A. S. Prigoda\*, V. V. Vereshchagin\*\* and A. G. Pokrovskiy\*\*, \*All-Union Scientific Research and Engineering Institute for Applied Biochemistry, Moscow; \*\*All-Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast; UDC 57.086.83]

[Abstract] HIV-1 producing Namalwa and MT-4 lymphoid cell lines were compared for growth rates on nutrient media with and without 10 percent fetal calf serum to assess the need of the latter for culture maintenance. The indices of proliferation of Namalwa and MT-4 cells on RPMJ-1640 medium with 10 percent fetal serum were 2.2 and 2.4, respectively. On a Soviet medium containing 1 percent bovine serum and 5 percent ultrafiltrate of pancreatic hydrolysate of casein the corresponding indices were 2.4 and 2.3. Metabolic studies with these media and serum-free RPMJ-1640 showed on the low-serum medium amino acid uptake is diminished without, however, a telling impact on cell growth. A consideration favoring the use of the Soviet medium is its ten-fold lower cost in comparison with RPMJ-1640 (West Germany). Tables 3; references 20: 9 Russian, 11 Western.

**Optimization of Large Scale Production of Blood  
Group-Specific Monoclonal Antibodies**

927C0300F Moscow BIOTEKHNOLOGIYA in Russian  
No 6, Nov-Dec 91 (manuscript received 12 Mar 91)  
pp 70-73

[Article by N. V. Proskurina, L. N. Lemeneva, Ye. I. Deryugina and I. L. Chertkov, All-Union Hematological Scientific Center, USSR Ministry of Health, Moscow; UDC 612.118.221.2.08]

[Abstract] (Wr x BALB/c) $F_1$  and (DBA/2 x BALB/c) $F_1$  mice were tested for their suitability in supporting growth of hybridomas producing monoclonal antibodies against blood group antigens. The results of extensive trials showed that optimum conditions for production of ascites with high antibody titers included irradiation of the mice with a 400 rad dose, priming with vaseline oil (in place of the expensive foreign product pristane), and intraperitoneal injection of 10E6 hybridoma A-86/44 cells (producing anti-A antibodies) or B-85/1 cells (producing anti-B antibodies). Fresh and lyophilized hybridomas were equally suitable. In the latter case DMSO did not have to be removed because of negligible toxicity, eliminating a difficult and time-consuming step. In general, 2.0 to 4.5 ml/mouse of ascitic fluid were harvested with titers ranging from 1:600 to 1:6400. Tables 6; references 9: 3 Russian, 6 Western.

### Disturbances in Immunity and Increased Fatigue Syndrome in Kievans

927C0188A Kiev VRACHEBNOYE DELO in Russian No 11, Nov 91 (manuscript received 06 Jun 91) pp 14-17

[Article by A. F. Vozianov, G. N. Drannik, I. A. Petrovskaya, and M. Ya. Musiy, Urology and Nephrology Institute, Ukrainian Ministry of Health; Molecular Biology and Genetics Institute, Ukrainian Academy of Sciences; UDC 612.017:616.8-009.17.352]

[Abstract] The immune system status was investigated in 1,030 essentially healthy adults living in Kiev and Kiev Oblast since the time of the accident at Chernobyl. These people were employed by various companies in the area. Approximately 700 worked under conditions of occupational hazards (antibiotics and other drugs, electrical gas welding, computers). Methods of quantitative and functional analysis of immune status parameters and tests that more accurately determine the functional activity of individual immune system populations were used. Analysis of immunograms from individuals with increased fatigue syndrome revealed a decrease in natural killer functional activity in 30 percent of these people. However, the remaining immunogram indexes were normal or elevated. Increased fatigue syndrome as identified by the authors is similar to the weak activity syndrome recently described by foreign authors. It is assumed to be an immunological disorder involving clinical signs of discomfort and fatigue that lasts more than six months and that can be treated with immunostimulants. The result showed that increased fatigue syndrome is associated with a decrease in natural killer activity, other clinical symptoms, and a change in the immunogram. It is most prevalent among those exposed to occupational hazards, especially antibiotics. The authors identified three stages characterizing various clinical and immunological indexes in the people under observation, to wit: 1. compensation stage, which is marked by wide fluctuations in immunological indexes with no signs of clinical pathology; 2. subcompensation stage, which is marked by alterations in the functional activity of immunocompetent cell populations and an increasing frequency of acute upper respiratory infections; and 3. decompensation stage, which is marked by depression of T- and/or B-cell immunity and secondary immunological insufficiency. These data indicate the importance of continuing research in this direction. The article recommends the organization of consultation offices for clinical immunology and municipal and oblast clinical immunology centers that can solve the problems of providing the public with specialized care in the diagnosis, treatment, and prevention of diseases with immunity disorders.

### Hematological Sequelae in Persons Exposed to Radiation at Accident at Chernobyl

927C0188E Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 36 No 8, Aug 91 (manuscript received 19 Apr 90) pp 31-37

[Article by A. K. Guskova and A. Ye. Baranov, Biophysics Institute, USSR Ministry of Health, Moscow; UDC 616.15-02:615.876/-07]

[Abstract] The objectives of this report were to: 1. describe typical changes in the peripheral blood for the first two months after exposure in 115 acute radiation sickness victims; 2. evaluate the impact of the modifying effect of  $\beta$ -burns on skin and bone marrow transplants on the blood index dynamics; and 3. project the possible remote stochastic effects of radiation on human hemopoietic tissue. The results demonstrated that peripheral blood count changes were typical of total uniform irradiation. The researchers noted regular restoration of myelopoiesis at gamma-radiation doses of six to eight Gy. Only six of thirteen victims given bone marrow transplants following exposure to external radiation of five to six Gy survived more than one month following the operation. The findings also indicated that signs of destructive processes in hemopoiesis develop only after exposure to 0.1-1.0 rad per day. In addition, the data suggested that actual pathogenetic mechanisms of transformation in hemopoiesis are closely associated with the dose, the uniformity of radiation of hemopoietic tissue, and the time between the onset of radiation sickness and the beginning of active reparative processes in hemopoiesis. The authors suggest that those who experienced acute radiation sickness (more than one Gy) may present with moderate cytopenia for the next one to three years and should be under dynamic observation. Most reparative processes will be completed within two to three years. This group of people may be at risk for developing leukemia. It is furthermore recommended that all cases of possible radiation exposure to doses of 0.1-1.0 Gy or more be recorded and the individuals in this group be under dynamic observation. Published data suggest that persons in this group are not at risk for developing leukemia. Figures 8; tables 1; references 23; 15 Russian, 8 Western.

### Analysis of the Effects of Radiation and Chemical Factors of the Environment on the Health of Newborns in the Vicinity of Nuclear Industry Enterprises

927C0326A Moscow GIGIYENA I SANITARIYA in Russian No 6, Jun 91 (manuscript received ) pp 50-53

[Article by L. A. Buldakov, S. N. Demin, E. R. Lyubchanskiy, Z. B. Tokarskaya, T. P. Fomina, I. A. Ter-novskiy (now deceased), V. A. Kolmogortsev, and A. G. Uralshin, Institute of Biophysics, USSR Ministry of Health, Moscow; UDC 614.73:621.039]:312.6]

[Abstract] In an attempt to determine the extent of the relationship between, on the one hand, chemicals and ionizing radiation and, on the other, congenital developmental effects and elevated morbidity and mortality in the neonatal period, the researchers here performed a retrospective study of newborns in areas in which effective equivalent dose exceeded 1 percent of the natural radiation background. The study included seven cities and seven rural areas, which accounted for a total population of 1,960,000. The data examined consisted of medical statistics for morbidity and mortality for 1978-1986, X-ray diagnostic reports for 1985-1987, reports of

releases of toxic substances for 1985-1986, and data on irradiation doses due to natural background and accidental releases. The chemical factors consisted of releases into the atmosphere of  $\text{SO}_x$ ,  $\text{NO}_x$ , and hydrocarbons from ferrous and nonferrous metallurgy plants. Multifactor linear regression analysis found no consistent link between the chemical or radiation factors and newborn health. A strong link was established between developmental defects and place of residence. The researchers also found that releases of  $\text{NO}_x$  and hydrocarbons were the biggest causes of death among the factors studied here. Morbidity was affected most by place of residence and releases of sulfur anhydride. Additionally, the researchers concluded that frequency of defects and morbidity rate were greater in cities. References 11: 9 Russian, 2 Western.

**Features of the Virulent, Antibiotic-Resistant Properties of Pathogenic Escherichia Circulating in the Environment**

927C0326B Moscow GIGIYENA I SANITARIYA  
in Russian No 6, Jun 91 (manuscript received  
12 Mar 90) pp 69-71

[Article by L. V. Grigoryeva, L. A. Malakhova, and T. G. Glushkevich, Republic Science Hygiene Center, UkSSR Ministry of Health, Kiev; UDC 614.718:[579.842.11:579.252.55].04:615.33]

[Abstract] Virulence and antibiotic-resistance were studied for 272 strains of pathogenic escherichia isolated from wash runoff, food products, waste water, reservoir water, drinking water, and soil in Ukraine. Some 79-95 percent of the strains exhibited a resistance to tetracycline, kanamycin, and streptomycin; 19-22 percent, to gentamycin and chloramphenicol. In terms of average MR, the following order was found: waste water (4.7) > food products (4.6) > soil (4.4) > wash runoff and reservoir water (4.1) > drinking water (3.5). That suggests that waste water, food products, and contaminated soil present the greatest risk for the spread of antibiotic-resistant strains. The researchers found, however, that wash runoff, waste water, and contaminated soil present the greatest danger in terms of aggressive strains with high virulence and antibiotic-resistance. References 15: 9 Russian, 6 Western.

**Evaluating Mutagenic Hazard of Environmental Pollution Based on Epidemiological Investigation of Miscarried Fetuses**

927C0247B Moscow DOKLADY AKADEMII NAUK  
SSSR in Russian Vol 321 No 1, Nov 91 (manuscript  
received 13 Sep 91) pp 203-205

[Article by Ye. N. Antipenko and P. L. Alekseyenko, Ukrainian Hygiene Research Center, Kiev; UDC 575.167:504.3.054]

[Abstract] This paper presents new ways of using epidemiological data from miscarried fetuses to evaluate the

mutagenic hazard of environmental pollution. The authors chose to use miscarriages as a factor for a number of important reasons: 1. the high value of the mutation component in their etiology; 2. significantly faster spread in comparison with other genetically caused events; and 3. miscarriages are much more sensitive to the environment. The investigation encompassed the years 1984-1987 using data compiled from all the gynecological hospitals in Simferopol, Zaporozhye, and Mariupol. Simferopol is a relatively unpolluted city while Zaporozhye and Mariupol each are quite polluted due to the heavily developed metallurgical industry. They each release an average of 414 and 916 thousand tons of toxic substances into the atmosphere each year, respectively, three to seven times more than in Simferopol. The results demonstrated that the average miscarriage rate was 1.4-1.8 times higher in polluted cities and that pollution-induced miscarriages occur three times more often in Mariupol and Zaporozhye. The length of residence in a polluted city was also shown to have a direct correlation with the incidence of miscarriage. In conclusion, the data demonstrate an increase in the mutation process in polluted cities. Tables 1; references 8: 4 Russian, 4 Western.

**Intensity of Mutation Process Among Residents of Cities With Different Levels of Chemical Pollution of Atmospheric Air (According to Analysis of Congenital Developmental Defects)**

927C0247C Moscow DOKLADY AKADEMII NAUK  
SSSR in Russian Vol 321 No 1, Nov 91 (manuscript  
received 13 Sep 91) pp 206-209

[Article by Ye. N. Antipenko and N. N. Kogut, Ukrainian Hygiene Research Center, Kiev; UDC 614.7:575.111:616-007]

[Abstract] The authors examined the rates of congenital developmental defects (CDD) in newborns from Simferopol, a relatively clean city, and from Zaporozhye and Mariupol, which are environmental polluted, for 1984-1987. Mariupol factories release 50 different substances with a total weight averaging 916 thousand tons each year. Fifteen of these substances are mutagenic. The newborns and children under one year of age were screened for 18 different CDDs. The ratio of these defects for Simferopol, Zaporozhye, and Mariupol was 1:2.3:3.1. The results demonstrated that the frequency of CDDs with dominant and X-linked inheritance in Mariupol was 3.1 times higher than in Simferopol. In addition, the rate of the mutation process was 1.2-2.1 times higher in Zaporozhye than in Simferopol and 1.5-2.6 times higher in Mariupol. Moreover, the frequency of dominant and X-linked CDDs was 2.2 times higher in Mariupol than in Zaporozhye. In conclusion, these results suggest that the environmental pollution in two cities in the Ukraine has considerably increased the rate of the mutation process. Tables 2; references 14: 8 Russian, 6 Western.

## Ecological Conditions in Russia 'Catastrophic'

927C0259C Moscow IZVESTIYA in Russian  
23 Jan 92 p 1

[Article by Vasiliy Kononenko, "Reactor of Nuclear Ship 'Lenin' Dumped Into Kara Sea"]

[Text] At a press conference held 22 January in the press center of the Old Square, A. Yablokov, the State adviser of Russia on ecology and public health, shocked the audience with his written statement that the ecological situation in Russian is close to a national disaster. Here are some excerpts from that document.

### Problem Areas

Officially, the zones of ecological trouble in Russian that have been designated to date are heavily contaminated regions resulting from the Chernobyl disaster, and also in the South Urals. These should include certain territories of Povolzhye, the Kuzbass, Central Yakutia, Priamurye, Krasnodar Kray, and the Kola Peninsula. Almost all republics, krays and oblasts could single out their own zones of ecological trouble and disaster.

Until now, little attention has been given to such an aspect of ecological trouble as the increased risk of technogenic disasters (ruptured pipelines, earthquakes that might be caused by pumping large amounts of water or petroleum from under the ground). For example, every year in our nation there are as many as 700 large breaks in oil and gas lines, and according to various estimates this results in a loss of from 7 to 20 percent of all recovered petroleum, i.e. tens of millions of metric tons. A. Yablokov emphasized that some international companies are interested even in recovering spilled petroleum, as well as residual fuel oil.

According to forecasts, as pointed out in the address, within 20 years, more than half of the territory of Moscow will be dangerously underflooded. Even now, 10,000-15,000 rubles per city dweller are being spent to save existing buildings. It is high time to develop a plan of precautionary steps based on general ecological certification of enterprises and territories.

### Life Has Been Shortened

The document also cites alarming figures about life expectancy in Russia. In 1964-1965, the average life expectancy was 70.4 years. At the turn of the decade between the eighties and nineties, the curve began to turn down, and in 1990 the figure was 69.3 years. Last year, 40 percent of the men who died were of working age. In some especially polluted cities, the average life expectancy is less than retirement age.

A. Yablokov also cited fresh facts: the life expectancy of peoples of small population in the North is 46-50 years, and according to data of Norwegian specialists, people in the city of Nikel live to an average age of only 44 years.

The State adviser also alluded to the scales of radiation contamination in Russia, which are not fully known. We are speaking of territories where nuclear explosions have been conducted for so-called peaceful purposes. There have been more than 120 of these, including more than 20 in the Volga Basin, 12 in Yakutia, and so on. There are only fragmentary data about serious contamination of territories as a result of production of nuclear weapons in closed cities: Chelyabinsk-6, Arzamas-16, Krasnoyarsk-45, Tomsk-7. According to A. Yablokov, we likewise do not know what is happening in the shallows of the Kara Sea, where the reactor of the nuclear ship "Lenin" has been buried (dumped into the water), nor at other nuclear waste burial sites. The Russian budget has allocated about 5 billion rubles this year to deal with radiation contamination. According to the words of the State adviser, the approach here is as follows: rather than to relocate masses of people, the approach is to decontaminate polluted territories wherever possible and to do total examinations of the populace. There are already good methods for this: to analyze blood or to analyze the structure of tooth enamel.

"Yet another danger that lies in wait for us" continued A. Yablokov, "is the imperfection of ecological legislation. For example, making natural resources subject to local agencies of authority often results in wanton destruction. (For the sake of comparison, let us note that the owner of timber land in France has no right to cut down a tree without appropriate permission from the agencies of authority.) Therefore, an urgent task is determination of the balance between the interests of the owner of private territory and of the entire State."

### There Is No One To Be Responsible

In answer to a question from the IZVESTIYA correspondent about development of a mechanism of protection against destruction of the environment, A. Yablokov noted that at this moment a new concept is being formed in that area. It is based on the principles of being subject to payment for the use of natural resources and payment for pollution and destruction of the natural environment. This is not a matter of fines for causal damage, but rather, as in all developed nations, compensation for harm done, which is immeasurably greater than any fine. However, a key factor in the state policy of rehabilitation of the ecological condition of Russia and improvement of the health of the people will be the realization of the right of each citizen to a healthy environment. In the United States, for example, 1500 people go to court every year against companies that have injured their health. Only a third of the suits are satisfied, but nevertheless, producers live, as it were, under a sword of Damocles, since the sums involved are enormous (to the point of threatening bankruptcy); this forces them to deal in a civilized manner. For the moment, we are the dirtiest residents in Europe says the state adviser, but he stressed that we will move along the path of developed nations.

**Heavy Metal Contamination of Soils in Kuzbass Urban Gardens**

927C0084A Moscow AGROKHIMIYA in Russian  
No 7, Jul 91 (manuscript received 04 Sep 90) pp 67-77

[Article by V. B. Ilyin, Institute of Soil Sciences and Agrochemistry, Siberian Department, USSR Academy of Sciences, Novosibirsk; UDC 631.416.8:581.19.6+641.1]

[Abstract] Garden soils in three urban settings (Novokuznetsk, Salair, Belovo) in Kuzbass were analyzed for heavy metal contamination to assess the health risk posed by local metallurgical plants. The results demonstrated that 92-100 percent of the soil samples contained elevated levels of Zn, Pb, Ni, Cr, Cu, and Cd, generally exceeding threshold limit values three- to 20-fold. The situation was particularly dangerous in the vicinity of a zinc smelting plant. In general, protective mechanisms precluded accumulation of dangerously high levels of the heavy metals in edible plant parts. However, tomatoes and cabbage tended to accumulate higher concentrations of heavy metals than beets and potatoes. Nevertheless, cadmium does pose a special risk category since it tends to accumulate to particularly high levels in plants. Figures 1; tables 3; references 9: 1 Polish, 2 Russian, 6 Western.

**Soil Forms of Cs-137 From Chernobyl Fallout in Various Areas**

927C0084B Moscow AGROKHIMIYA in Russian  
No 4, Apr 91 (manuscript received 19 Jun 90) pp 84-86

[Article by L. V. Surkova and R. I. Pogodin, Chelyabinsk Branch, Institute of Biophysics, USSR Ministry of Health; UDC 631.41:546.36]

[Abstract] In order to improve estimates of bioavailability of Cs-137 in the territories affected by the Chernobyl accident, soil samples in Ukraine and Belarus were analyzed for Cs-137 levels in 1987 and 1988 within a 250 km radius. The results showed that three years after the accident approximately 55-79 percent of Cs-137 is fixed and refractive to leaching with 6 N HCl. In addition, the highest percentage of fixed Cs-137 is found within the 30 km zone and evidently is due to fallout of heavier, poorly soluble fuel particles. Over time Cs-137 levels diminish in direct proportion to the distance from the power plant: 1.2- to 1.3-fold within 30 km and 1.7- to 3.0-fold at greater distances. The rate of Cs-137 fixation for the different soil types ranks as follows: bog peat > sandy dernovo-podzolic > loamy dernovo-podzolic. Rate plots indicated that completion of fixation for Cs-137 will require five to 10 years, depending on soil type. Figures 1; tables 4; references 6 (Russian).

### Tuberculosis Threat Increases

927C0265C Moscow VECHERNYAYA MOSKVA  
in Russian 10 Jan 92 p 2

[Interview with Professor Aleksey Alekseyevich Priymak, director general of "Phthisiopulmonology" Practical Science Association, Russian Ministry of Public Health, by B. Yakovlev; place and date not given: "X-Raying Next to the Tavern. Professor A. Priymak, Director General of 'Phthisiopulmonology,' Warns: Tomorrow Will Be Too Late"]

[Excerpts] A truck carrying an X-ray machine (fluorograph) drove up to the tavern, where about fifty people were milling about. Doctors had warned that public houses would be immediately closed up unless everyone here assembled were examined for tuberculosis, anonymously if so desired. Result? Five ill with tuberculosis who had, of course, been so warned. As to the careful washing of glasses, or the brotherly sharing of one glass by three people, all the sanitation and hygiene of our taverns, and incidentally not just taverns, the reader needs no details: All that is well known...

[Priymak] About forty thousand people in Russia come down with tuberculosis every year, and nine thousand die. These are the latest data, and the figures are persistently increasing. Unless decisive steps are taken, tomorrow will be too late.

In these difficult times, we might not notice a dreadful disease in time, let it pass, and thereby put the peoples of Russia on the edge of survival. We overcome political and economic adversities, and then we suddenly notice with horror that we are in the grip of a tuberculosis epidemic, that the gene pool of Russia is threatened. [passage omitted]

First of all, it must be publicly acknowledged that we are being stricken once again with tuberculosis and that we may be threatened with an epidemic.

At the risk of sounding old-fashioned, I nevertheless emphasize that our Moscow Scientific Research Institute of Tuberculosis was set up at Lenin's order on the first anniversary of the October Revolution. It was one of the first specialized medical institutes of Russia at that time. Its establishment showed an understanding of the danger threatening the nation.

In general, we have had a long (two centuries) and instructive history.

The institute is housed in the Mariinskiy Hospital constructed as a Founding Hospital. The charter states that its doors are open to all who come and ask for help. At that time, the street was called Novaya Bozhedomka: God's Home. One hundred seventy years ago, a son Fedor was born to the family of Doctor Dostoyevskiy who then lived here.

During the War of 1812, at first we had a hospital for Russian soldiers, and then when the enemy had invaded

the country, a French hospital was opened next door. The Russian physicians did not leave with their retreating army, and the French brought bandages, medicines, food, and even offered to decorate their colleagues for bravery, but the latter refused, saying that they were merely fulfilling the hospital charter. The city fire bypassed this place. When Napoleon retreated from Moscow, their hospital was still here, and the Russians furnished their neighbors with provisions.

So when we talk about the history of civilization, we ought to remember this fact, and think about whether we have strayed far, and to what side... Put my brief historical digression under the topic: civilization and tuberculosis.

[Yakovlev] Is it curable?

[Priymak] Certainly! If a very small part is given over to surgeons as well, then practically one hundred percent. Treatment used to take two to three years; now, by using our recently proposed technique, it can be managed in a matter of six to eight months.

[Yakovlev] Then cure away! Why talk about the threat of an epidemic?

[Priymak] First there has to be a diagnosis. The diagnostic methods themselves—X-ray and bacteriological—are diverse and precise, and they are being improved by "Phthisiopulmonology" and its subsidiary, the Moscow Scientific Research Institute of Tuberculosis, working on a broad front, from setting up mobile X-ray facilities together with the Hungarians, Czechs and our defense enterprises, to the development of a refined method of immuno-enzymatic diagnosis that is safe for bacteriologists (many of whom become infected themselves from contact with the tubercle bacillus). Our gas-liquid chromatography shows promise.

The root of the evil is not in the problems of diagnosis, but rather something else altogether: our inborn slipshod ways. For the sake of comparison, consider this: Germany uses the fluorograph four times as intensively as we do. There almost everyone regularly goes through an examination. On the other hand, my dear compatriots set great store on the off-chance, and sidestep the entire easily accessible procedure.

[Yakovlev] No one has any use for X-rays.

[Priymak] Negligible exposure means negligible danger. By avoiding it you take a risk one hundred times greater...

Tuberculosis has already shown us its "portrait" of the group at risk. Generally uncultured people without much education, getting minimum average pay. And incidentally, this has always been the case. I recall thirty odd years ago when I began working as a physician in the tuberculosis unit of the hospital, I left home in the mornings carrying a bag of groceries to supplement the diet of my patients.



[Yakovlev] These days, the doctor's grocery bag is almost empty.

[Priymak] When it comes to tuberculosis, a good protein-rich diet is also medicine. In spite of economic tempests, we are doing our best to stand firm: to feed our patients with better and tastier food. Our hopes are pinned mainly on inventive cooks, rather than on providers of supplies. However, galloping inflation may undermine this measly prosperity...

Another risk group comes from dusty, smoky shops, night shifts that upset the human biological clock just like stresses, and therefore weaken the immune system, opening the way to infection. Tuberculosis is often linked with some other complaint, such as barrenness: cure one, and the other comes through.

Of particular concern are children. In maternity hospitals, everyone is inoculated against tuberculosis. Boosters are mandatory (our institute has done research to determine the optimum times). Do your best to keep children as far as possible from overcrowded transport, out of contact with coughing relatives, friends and neighbors. Do not hesitate to visit the doctor again if you are concerned because your daughter or son is not feeling well.

[Yakovlev] Are you intentionally leaving out prison inmates as a special risk group?

[Priymak] No! That is no longer a taboo subject, and it has always been an urgent one for us. We have even organized a special laboratory at the institute. Central funding for the project has now been cut off, but we are still finding some financing.

I tell you without exaggeration: The zones are in the grip of a tuberculosis epidemic. The illness is 30-40 times more prevalent there than on average in Russia, and deaths are ten times more frequent, even though there are exceptions to this dismal rule. I recently visited a camp in Yakutia and met a doctor who would have done credit to Moscow, the situation there is better.

Of course, tuberculosis in and of itself in the zones is far from a mere medical problem, and has to be solved jointly by many agencies.

[Yakovlev] A man gets out of prison...

[Priymak] Let me continue your thought. A patient with an open form of tuberculosis infects about twenty healthy people in a year. There is considerable neglected tuberculosis among prostitutes, and slack registration allows them to circulate about the country practically unimpeded. So you see, democracy has its flip side.

[Yakovlev] Do we clamp down again, increase prohibitions?

[Priymak] It is time to pass a special law on tuberculosis that defines the rights and obligations, the responsibilities of the patient and doctor.

Upon release from prison, arrangements for employment must be accompanied by a mandatory examination, and if treatment is evaded, it must be done forcibly. In this respect, tuberculosis can be likened to AIDS and sexually transmitted diseases.

[Yakovlev] None of our prohibitions have yet cured any illness.

[Priymak] Some are inadequate, but you cannot manage without them. A healthy person has a right to protection from those who do not care about themselves or anyone else.

Legislative measures are only part of the anti-tuberculosis program that Russia must have.

[Yakovlev] It has often been said that the boundaries between former republics will be "transparent." Does it make sense to confine the program to Russia alone? These arbitrary boundaries are no barrier to the tubercle bacillus.

[Priymak] My dream is that it will unite the forces of the entire Commonwealth of Independent States.

We have experience in such work, and it would be a crime to shirk it. For example, our "Phthisiopulmonology" is actively helping in the fight against tuberculosis in Kazakhstan, where the illness is more prevalent than in Russia.

[Yakovlev] Is a special program needed for Moscow?

[Priymak] My feeling is that there is such a need.

We have to start by getting a realistic picture, because the seemingly safe local figures have to be carefully checked. It might be a good idea to resurrect the interagency commissions on tuberculosis that formerly were affiliated with district executive committees; they could now be affiliated with prefects. Let us recall the forest schools for small children. Anything that was useful in the past should be given new birth.

Whether things are good or bad with regard to tuberculosis is the calling card of any authority. Tuberculosis is not under good control right now here in Russia, and if we stick our heads into the sand as before, it will be uncontrolled.

### **Possibilities of Long-Range Prediction of Influenza A Pandemics**

927C0301A Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 5, May 91 pp 27-30

[Article by G. P. Zhulova and V. A. Orlov, All-Union Influenza Scientific Research Institute, USSR Ministry of Health, Leningrad; UDC 616.98:578.832.1036.22-037]

[Text] We are presently unable to make any long-term predictions of influenza epidemics that would answer



the question as to when and where the next pandemic would arise and what serological subtype of influenza A it would be evoked by, inasmuch as we do not know whether the number of influenza agents is limited, what the patterns of their appearance in the epidemic arena are, and whether or not there is a link between epidemics and other natural phenomena.

Using a large quantity of factual material, A. L. Chizhevskiy demonstrated a mutual relationship between epidemics of plague, cholera, smallpox, influenza and other diseases and solar activity<sup>17</sup>. He revealed by retrospective analysis a periodicity of influenza epidemics that coincides somewhat with the 11-year cycle of solar activity. Using 11-year cyclicity to predict influenza epidemics, V. N. Yagodinskiy was able to predict the Hong Kong flu pandemic of 1968-1969, but predictions of subsequent epidemics were unsuccessful<sup>18</sup>. It is apparent that influenza epidemic predictions cannot be based solely on solar activity. V. Z. Soloukhin proposed basing predictions on fluctuations in the hydrobiological cycle of northern seas, which influences the vital activities of plankton, which in the author's opinion is the main reservoir of influenza virus in nature<sup>16</sup>. Soloukhin marked the dates of appearance of influenza epidemics in the 20th century on the curve describing variations in the hydrobiological cycle of the Barents Sea, and showed that viruses of serological subtypes A(H2N2) and A(H3N2) appeared in the "cold" period, A(H0N1) and A(H1N1) appeared in the "moderate" period, and A(HswN1) appeared in the "warm" period. Nonetheless he relied in his prediction chiefly on the 11-year cycle of solar activity, "during the maximums of which people are subjected to regular pandemics of influenza A"<sup>16</sup>. According to the author's prediction the next "Spanish flu" pandemic should have occurred in 1988, but this prediction was not confirmed either<sup>17</sup>.

Thus while Chizhevskiy and Yagodinskiy tried to answer the question as to when the next epidemic would arise, Soloukhin wished to answer the question as to not only when an epidemic would arise but also what virus it would be evoked by.

In contrast to Soloukhin, we believe that the human population is the main reservoir of human influenza virus in nature. For reasons still unknown, the precursors of major epidemic events are among populations of countries in the Earth's southeastern region<sup>11, 15</sup>. We attempted to obtain an answer to all three questions of a long-range prediction: Where will the next pandemic arise, and when and by what serological subtype of influenza virus will it be evoked? Our prediction was based on data on the cyclicity of pandemic activity of human influenza A virus, viewed as a single global epidemic process with its epicenter in the southeastern region<sup>11</sup>. The complexity of the cyclicity of these events manifests itself in the fact that every 10-18 year pandemic cycle includes three to five epidemic cycles, as well as in the fact that one pandemic cycle may include major epidemic events evoked by two precursors, for example viruses A(H3N2) and A(H1N1). The epidemic activity of

the precursors differs, since not all influenza A viruses of known serological subtypes capable of initiating a pandemic cycle evoke the largest epidemic events qualified by epidemiologists as pandemics. Thus, virus A(H0N1), which initiated a pandemic cycle in 1929, did not evoke significant epidemic events in the same way that virus A(H1N1) did when it began circulating in 1947<sup>1, 15, 19</sup>.

Basing ourselves on the different epidemic activity of precursors, which manifests itself in different levels of morbidity, severity of clinical course, and mortality, in our retrospective analysis we accounted only for the largest epidemic events categorized as pandemics. According to data of epidemiologists<sup>1, 5, 17, 19</sup> there were a total of 13 pandemics between 1675 and 1990: in 1675, 1693, 1732, 1779-1781, 1802-1805, 1829-1830, 1847, 1857, 1889, 1918, 1957, 1968 and 1977. A southeastern origin was demonstrated for 10 out of 13 of them (this region includes the southeastern areas of Siberia). An epicenter was not precisely established for the remaining three (1675, 1693, 1732). There are conflicting reports regarding the exact times of appearance of pandemics (to the month) in the literature. Thus according to Beveridge five pandemics arose in the spring and summer months (March 1847, May 1889, March, August 1913, August 1857, July 1968), and five arose in the fall-winter season (October-November 1732, fall 1781, September-October 1800, January 1830, February 1957<sup>19</sup>). According to data of other authors pandemics arose in July 1675<sup>1</sup>, July 1968<sup>12</sup>, May 1977, February 1889<sup>15</sup>, March 1957<sup>15</sup> and October 1917<sup>1</sup>. Our analysis of the data of the last 20 years showed that the precursors of major epidemic events appeared in the southeastern region from April to June—serological subtype A(H1N1)—and from July to September—serological subtype A(H3N2)<sup>11</sup>.

The sole case thus far of precise documentation of the precursor and the beginning of the pandemic it evoked was noted in 1968, when it was reported that growth of influenza-like illness was noted on 12 July in the southeastern part of China and on 13 July in Hong Kong, and that on 17 July A/Hong Kong/1/68 (H2N2) influenza virus was isolated<sup>12</sup>. However, the precursor of the next pandemic, which began in China in May 1977, was not revealed promptly, and its beginning was associated with influenza A(H1N1) virus, which was not isolated until six months later in the USSR<sup>12</sup>. These data indicate the need for careful and prompt screening of the precursors of pandemics and major epidemic events in the southeastern region.

The means by which the five main serological subtypes of human influenza A agent survive and alternate remain unclear. Information on the periods of circulation of these serological subtypes was obtained on the basis of serological archeological (1889-1933) and virological (1933-1990) data. According to these data A(H2N2) virus circulated in 1889-1899, A(H3N2) circulated in 1900-1917, A(H1N1) circulated simultaneously from 1909 to 1917, A(HswN1) circulated in 1918-1928, A(H0N1) circulated in 1929-1946, A(H1N1) circulated

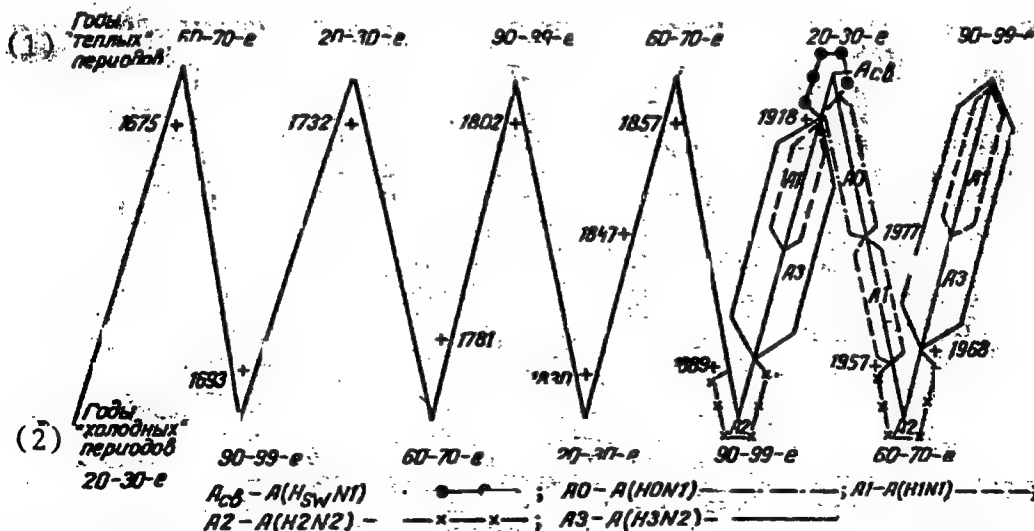
in 1947-1956, A(H2N2) circulated in 1957-1967, A(H3N2) circulated in 1968-1990, and A(H1N1) circulated simultaneously from 1977 to 1990<sup>15-21</sup>.

We compared data on influenza pandemics with long-term cyclic changes in the climate of the Northern Hemisphere. Long-term cycles of climatic change described in a major work by Bruckner covering a 900 year period<sup>20</sup>, and confirmed in the 20th century<sup>3, 4, 8, 10, 13</sup>, include three successions of "cold" and "warm" periods in a century within practically the same decades between the twenties and thirties, the sixties and seventies, and nineties to the end of the nineties<sup>20</sup>. We plotted the dates of pandemic activity of influenza A viruses on the temperature curve from 1675 to 1990 (see figure). It is evident from the figure that all peaks of the curve—the extremes of the "cold" and "warm" periods—were occupied by pandemics, and only two of the 13 pandemics occurred in intervening periods. In this case serological subtype A(H2N2) pandemics were localized at the extremes of the "cold" periods of the 20th century, while Spanish flu was localized at the extreme of the "warm" period of the 20's-30's, which is consistent with Soloukhin's data<sup>7</sup>. A(H1N1) virus appeared three times in the epidemic arena, in which case it circulated twice simultaneously with A(H3N2) virus, joining it nine years after its appearance, and both times the period of circulation occurred on an ascending segment of the temperature curve. Subtype A(H0N1) virus appeared only once, failing to evoke major epidemic events, and the cycle it initiated localized itself on a descending segment of the curve at an interval of 11-12 years after the Spanish flu.

In Bashenin's opinion<sup>1</sup> the 1675 pandemic, which is located on our diagram in the zone of a "warm" period,

had astounding similarity to the Spanish flu pandemic, which "was related to the neurotoxic type" and which primarily afflicted people in their prime, in contrast to the 1889 "catarrhal-pulmonary type" pandemic, which afflicted the elderly and children and which is located in our figure in the zone of a "cold" extreme. Thus the impression is created that Spanish epidemics regularly confine themselves to the extremes of "warm" periods, while "Asian" pandemics elicited by A(H2N2) viruses confine themselves to the extremes of "cold" periods. Extremes span an entire decade.

The succession in which different serological subtypes of human influenza A virus appear in the epidemic arena cannot be said to be random. A profound mutual relationship between agent and host populations, regulated by biological rhythms in the epidemic activity of the virus and the immune status of the macroorganism, is reflected in this process. These biorhythms have a complex cyclicity that includes a large cycle around 100 years long (for example from 1889 to 1991), which consists in turn of three 33-year cycles ending with the severest "Spanish" and "Asian" flu pandemics (in this case either two Spanish flu and one Asian flu pandemics may occur in a 100 year cycle, or vice versa), and 10-12 year cycles initiated by a certain sequence of viruses A(H0N1), A(H1N1) and A(H3N2). Thus one century cycle includes three 33-year and nine 10-11 year cycles. Indirect evidence of the existence of biological rhythms associating man with influenza virus can be found in our opinion in the astounding coincidence of the dates of appearance of pandemics and major epidemics in the same decades of different centuries: 1557, 1657, 1857, 1957; 1647, 1847, 1947; 1675, 1775, 1977; 1427, 1627; 1688, 1788; 1602, 1802; 1737, 1936.



Cyclicity of Long-Range Changes in Climate of the Northern Hemisphere and Influenza A Pandemics: The curve is a schematic representation of changes in the climate of the Northern Hemisphere over 315 years, with the extremes of the "warm" and "cold" periods in the corresponding decades (twenties to thirties, sixties to seventies, and nineties to the end of the nineties) indicated; 1675+, etc.—dates of appearance of influenza A pandemics.

Key: 1. Years of "warm" periods 2. Years of "cold" periods

The severest pandemic of a "warm" period—one of Spanish flu that took 20 million lives and supposedly began in China<sup>5</sup> in October 1917<sup>1</sup>, coincided with a peak of solar activity, manifesting itself as a huge protuberance recorded on 7 July 1917<sup>17</sup>. If we take as our point of reckoning July 1917 and associate emergence of the precursor of Spanish flu into the epidemic arena with it, and the beginning of the pandemic with October 1917, then the 3-month interval between them has prognostic significance.

Of 13 pandemics, only 9 have occurred in a period of minimum solar activity, while 11 have occurred at times of maximum activity<sup>6,17,18</sup>. We are presently at the extreme of a "warm" period, with the proposed peak of solar activity occurring in 1991.4  $\pm$  1 year<sup>14</sup>. The modern period is similar to the period preceding the Spanish flu not only in terms of climatic and solar data but also in terms of the virological situation: A(H1N1) and A(H3N2) viruses are circulating simultaneously on an ascending segment of the temperature curve in precisely the same way (see figure). Consequently we can predict with significant probability that the next influenza A pandemic will be elicited by a virus related in biological and antigenic properties to the precursor of Spanish flu.

Analysis of data on the beginning of 13 pandemics revealed that 11 (85 percent) of them coincided with years of maximum or minimum solar activity (as determined by Wolf numbers), and only two preceded maximums of solar activity—by one year in 1847 and by three years in 1977<sup>9,17,18</sup>. Thus the greatest probability of appearance of the precursor of a recurring pandemic is in the year of the anticipated maximum of solar activity. According to available data the mean annual Wolf numbers were 13 in 1986, 29 in 1987, 100 in 1988, 150 in 1989, and in 1990 an increase to 173  $\pm$  17 is anticipated. As was noted above, a peak of solar activity is highly probable in 1991, and a peak of low probability is possible in 1990 and 1992. Consequently considering the mutual relationship between pandemics of preceding years and peaks of solar activity, and on analogy with the conditions under which the Spanish flu appeared, advent of the precursor of the next pandemic is most probable in July 1991 in countries of the southeastern region, and the beginning of the epidemic process is most probable in October 1991. However, there is a certain probability that pandemics will also occur in 1990 and 1992. Inasmuch as the extreme occupies an entire decade, a more accurate prediction would be possible only upon attainment of the peak of solar activity.

Thus according to our prediction the next influenza A pandemic will most probably be expected in 1991; its precursor, which is related in biological properties to the agent of Spanish flu, should appear in the southeastern region (most likely in China) in one of the summer months, and the beginning of the epidemic process should be expected three months later.

Basing ourselves on the biological rhythms we revealed in epidemic activity of influenza A virus in their relationship to cyclicity of climatic and solar changes, we propose the following long-term prediction: After the pandemic cycle of 1991-2002 comes to an end, the first thing we should expect in the descending segment of the curve is the appearance of A(H0N1) virus, which will not evoke major epidemic events; then a 9-10 year cycle should follow, associated with circulation of A(H1N1) virus, and by the time of the next extreme of the "cold" period in the twenties to thirties, an A(H2N2) pandemic will begin. A more precise long-term prediction of the largest epidemic events requires consideration of solar activity in the indicated years, desirably with the additional consideration of the effects of other heavenly bodies—Jupiter, Saturn, Uranus etc.<sup>2, 17</sup> Thus making a long-term prediction of influenza pandemics involves consideration not only of the biological patterns of influenza agent but also the influence of different planetary and cosmic factors upon the biological rhythms in the epidemic activity of the agent.

If we have accurately revealed the patterns of the bio-rhythms in the pandemic activity of influenza A virus, and if this is confirmed in the current extreme of the "warm" period at the peak of solar activity, then the conception presented here could be used to predict influenza pandemics not only in the immediate but also in the remote future.

The conception of prediction of influenza pandemics presented here is the personal point of view of the authors, and it does not reflect the official position of the All-Union Influenza Scientific Research Institute of the USSR Ministry of Health in regard to this problem.

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### Review of Book on Cholera Surveillance in the USSR

927C0301B Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 5, May 91 pp 79-80

[Review by A. Ye. Essel of book *Epidemiologicheskiy nadzor za kholeroy v SSSR* [Epidemiological Surveillance of Cholera in the USSR] by G. M. Medinskiy, M. I. Narkevich, V. P. Sergiyev and A. K. Adamov, Moscow, Meditsina, 1989, 5,700 copies, 141 pp; UDC 616.932-036.2-084.4]

[Text] The seventh pandemic of El Tor cholera is not only interesting in its scope and duration, but it also differs from preceding pandemics in the biovar of the agent. Biological and ecological features of El Tor cholera vibrios and accelerated spread of disease in a number of countries and on different continents necessitated critical analysis of measures being implemented, including by the epidemiological surveillance system. The monograph reviewed here is devoted to experience accumulated in the USSR in maintaining surveillance over cholera, with additional data cited from the world literature.

Chapter one examines features of the occurrence of cholera today. The authors make a detailed analysis of the chronology and geographic distribution of the seventh pandemic, focusing attention on the rate of spread, which is incomparable with that of previous epidemics. Analyzing the causes of formation of secondary foci, the authors validly emphasize the significance of resistance, of the agent's broad adaptability, which manifests itself as its lengthy survival outside the human body, and finally, of variability, including L-transformation.

Countries of the African continent are used as an example to persuasively demonstrate that under certain conditions the factors of socioeconomic development may promote deterioration of the epidemiological situation.

Chapter two examines the epidemiological aspects of the ecology of cholera vibrios. While I agree with the general summary of basic premises, I believe that the assertion of the authors that cholera vibrio is "one of the most graphic models for the study of evolutionary plasticity" (p 14) is too categorical. Such an assertion requires synecological grounds of greater validity than those offered by the authors. Data on "directed" change in the properties of pathogenic enterobacteria in the immune organism (V. L. Yelin, O. P. Rozenblat, 1937) are obsolete, all the more so because vibrios are not enterobacteria.

Descriptions presented in the book of strains isolated from patients and vibrio carriers, as well as from various objects, including aquatic organisms, are interesting. Data on vibrio survival are especially significant. An overall analysis reveals that not only man but also other objects can serve as ecological niches for cholera vibrio. At the same time conclusive answers are not found for questions regarding the maximum time of survival of vibrios, and concerning the forms in which microorganisms persist in different ecological conditions. L-transformation is of special interest in this aspect. Detailed materials are presented on survival of cholera vibrios in water basins with different ecological characteristics. The question of the epidemiological significance of cholera vibrios with altered properties, especially with reduced virulence, is of great practical and theoretical interest.

The general conclusion is basically that in conditions where avirulent and weakly virulent strains circulate, spontaneous infection of the population is not accompanied by pathological manifestations and immunological shifts. This justifies limiting the volume of epidemic control measures.

Chapter three is devoted to the theoretical aspects of epidemiological surveillance over El Tor cholera. The authors validly note the ambiguity in the definition of the concept of "epidemiological surveillance," and they view it not only as analysis of the dynamics of infectious morbidity, of the age, sex and occupational composition of patients, of the biological and ecological features of the agent, and of the pathways and conditions of its transmission, but also as the planning and implementation of specific measures to reduce morbidity or eliminate the epidemic. In this case not only is a definition offered for the concept of "cholera focus," but also the definition of a "focus boundary" is refined. It is noted that implementation of a full complex of preventive and epidemic control measures against cholera requires a developed public health infrastructure, a population with high general and public health knowledge, and significant material outlays.

The authors provide specific recommendations regarding bacteriological testing associated with protecting the land from importation and spread of cholera. It is noted in particular that positive results of bacteriological tests on people arriving from countries with a high cholera risk are usually recorded only among those suffering gastrointestinal disorders, or those who had been subjected to the risk of infection during their presence right within an infection focus, if a period of time equal to the incubation period had not passed after this. This approach raises the probability of isolating vibrios, and it makes it possible to significantly reduce the quantity of unjustified bacteriological testing.

Chapters four and five examine problems concerned with the tactics of public health and quarantine measures in relation to persons coming from places with a high cholera risk, and they present the general principles of quarantine and confinement measures. Substantiations are offered for a complex of cholera control measures which are not inferior to quarantine measures in their effectiveness but which require significantly lower outlays and which do not essentially disturb economic activity.

Chapter six presents and substantiates the tactics of epidemiological surveillance in cholera foci. Measures conducted within the population with regard for its occupational distribution and the objects subject to bacteriological testing are examined successively. Special attention is devoted to testing environmental objects, and surface water basins in particular.

Chapter seven presents materials on temporary hospitalization, on active detection of patients with acute intestinal diseases in cholera foci, and with emergency preventive treatment with antibiotics depending on the risk of infection.

Summarizing published data and personal experience, the authors point out that an increase in the number of patients with acute intestinal infections in specific population centers, especially along the shores of southern seas and rivers, which attract large numbers of vacationers in summer, is an indication for intensifying epidemiological surveillance for cholera. Temporary hospitalization is indicated when patients are revealed with warning signs (diarrhea, vomiting). In these cases a minimum of three repetitions of bacteriological tests are conducted in the very first hours (prior to administration of antibiotics). The authors thoroughly substantiate the significance of temporary hospitalization and of active detection of patients in a cholera focus to epidemic control.

Special attention is devoted to emergency preventive treatment of cholera with antibiotics. The authors name tetracycline, levomycetin and chloramphenicol among the most effective drugs for treating cholera. It should be noted that the latter are synonyms. The results of experiments and clinical research have substantiated the choice of tetracycline and chloramphenicol for emergency preventive treatment of cholera. Unfortunately, in their analysis of the effectiveness of antibiotic therapy and antibiotic preventive treatment of cholera, the authors do not examine the influence of the corresponding drugs on the microbial community of the gastrointestinal tract. Disturbance of the latter (both qualitatively and quantitatively) can lead to many consequences, particularly to a relatively long period of elimination of disease agents by recovering patients treated with antibiotics. Nor is the influence of these preventive measures on immune status examined.

Chapter eight discusses the tactics and organization of cholera control measures in the season between epidemics. The authors turn special attention to the time cholera vibrios remain within the human body. Lengthy retention of vibrios is recorded extremely rarely. In this connection it would be reasonable to reduce the time of dispensary observation of recovering patients, and to group them with persons under observation for chronic diseases of the liver, gallbladder and bile ducts. Testing of environmental objects for cholera vibrios and proper selection of such objects and the sampling points acquire special significance.

The "Instructions on Organizing and Conducting Cholera Control Measures" (12 September 1983), an appendix discussing disinfection procedures and the disinfectant consumption norms, and a list of methods and instructions are useful supplements to the book.

On the whole despite certain omissions this short monograph will be useful in general theoretical and applied



respects not only to epidemiologists, microbiologists, infection specialists and public health organizers, but also to specialists in gastroenterology and instructors in the appropriate departments of medical institutes.

It would be desirable to republish the book in larger numbers.

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### Modern Problems of Epizootology

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[Article by I. A. Bakulov, All-Union Scientific Research Institute of Veterinary Virology and Microbiology; UDC 619:616.9]

[Excerpts] [passage omitted] Competently utilizing the accomplishments of science, our country's practical specialists have managed to gain control over epizootics, eliminate many especially dangerous infectious diseases and sharply restrict the incidence and the harm done by a large number of other infections and invasions.

However, the complete well-being of livestock farms has not been ensured everywhere in our country in regard to diseases such as tuberculosis, brucellosis, leptospirosis, listeriosis, Aujeszki's disease, classical swine plague, swine erysipelas, Newcastle disease, salmonellosis, pasteurellosis and others, despite the numerous government decrees, timetables and promises.

The world epizootic situation also remains extremely explosive. This tension is especially high in Africa, Asia and South America. Especially dangerous diseases such as cattle plague and contagious pleuropneumonia are still widespread on the African continent, while glanders still occurs in certain Asian countries. Cattle plague also occurred in the not-to-distant past in states contiguous with our country (Iran), and in Europe, an enormous focus of the most dangerous disease—African swine fever—presently exists in Spain, Portugal and Italy (Sardinia), from which this disease has been carried on several occasions to France, Belgium, the Netherlands, and probably Brazil and Cuba. For practical purposes we are presently dealing with a panzootic of African swine fever. Each year several hundred unfavorable foci of contagious cattle pleuropneumonia are revealed in Portugal. The situation remains tense for the time being, with over 1,000 foci established in 1989.

A viral disease that is completely new to us has achieved panzootic occurrence—viral hemorrhagic disease in rabbits. It appeared for the first time in Asia (China), then in Europe and the Soviet Union, and now it is being recorded in Mexico and the USA.

Concurrently with this, a disease with a similar complex of symptoms, called the "brown liver syndrome," was detected in rabbits in many European countries (Italy, FRG, France, Denmark, Sweden etc.). It was established

that it is evoked by *Calicivirus*, which is kindred to but differs from hemorrhagic disease virus.

*Parvovirus* infection of dogs should also be called a panzootic: It has spread throughout all continents. It is believed that the agent originates from the closely related feline panleukopenia virus. This category also includes *Paramyxovirus* infection of pigeons, which has evoked mass die-off of gallinaceous birds. [passage omitted].

New infectious animal diseases formerly unknown to science and practice have appeared (and perhaps, developed). Several diseases of horses can be named among them: Potomac River disease, of which bacteria of genus *Ehrlichia*, order Rickettsiales are the agent; contagious metritis, a disease that is bacterial in origin; Get's [transliteration] disease of viral etiology. Antibodies to human legionellosis agent have been detected in horses, and *Legionella* has also been isolated from calves.

Entirely new, formerly unknown diseases are also appearing in other species of animals—spongiform encephalopathy in cattle and cats, and the "blue eye syndrome" in pigs.

Special emphasis should be laid on a unique feature of modern pathology: the dominance of paramyxoviruses appearing as epizootics among pigeons, the "blue eye syndrome" and *Paramyxovirus* infection of seals.

Some infectious diseases which were just very recently believed to be exotic in our country have now been detected on USSR territory as well—Teschin disease and myxomatosis for example.

Continually expanding international relations carry the threat of importation of agents of dangerous diseases into our country. The nature of modern communication resources favors this to a certain degree. [passage omitted].

We need to make a transition in veterinary medicine to a system of constant, intensified veterinary surveillance over the state of animals irrespective of the presence or absence of infectious diseases, and toward constant methods of assessing the epizootic situation, including by means of sero-allergic and other testing methods. The microbial environment and the succession of agents (change in antigenic and other characteristics) should be constantly monitored, warning of the development of epizootics must be provided, and changes in the epizootic situation must be detected at the earliest stages of the appearance and spread of diseases, which will make it possible to effectively and purposefully conduct epizootic control measures.

Work of this kind will require creation of a unified system for collection and computer processing of statistics, and it will require the use of computers. Closely related to this is the problem of mathematical modeling and prediction of the development of the epizootic process and of changes in the epizootic situation, which

will in turn make it possible to implement preventive and epizootic control measures more promptly and effectively.

Unfortunately, Soviet science is significantly behind in the study of the subtle structure of disease agents, and chiefly in studying the genome of viruses and mapping its segments, which makes it impossible to use new methods of genetic engineering to differentiate between epizootic and vaccine strains, and consequently to develop effective programs of disease eradication. [passage omitted].

The epizootic process in livestock breeding, especially in industrial type farms, is another matter. In this case man's intervention is considerable and constant—in raising animals, grouping and moving them, and so on. All of these actions are purposeful rather than matters of chance. Therefore in this case it would be more proper to discuss the social, or more accurately the biosocial nature of the epizootic process in modern livestock breeding.

Another task of epizootologists is to develop state programs to prevent and control infectious diseases. We still do not have a unified program of preventive and epizootic control measures against especially dangerous infectious diseases (such as the program developed in the USA). At the same time especially dangerous diseases, including those exotic in our country, continue to be a serious threat. They must be studied from the positions of general and particular epizootology. The list of these diseases is extremely impressive. The damage they inflict in primary foci may be enormous.

This is a good time to raise the question of creating a quick response service, including in veterinary medicine.

Special attention should be turned to the problems of differential diagnosis. In a number of cases we are well aware of some specific disease, but we have a poor knowledge of the problems of differential diagnosis (in which we also instruct students poorly), despite the fact that this is the most important tool of an epizootologist.

Infectious pathology is also diverse in our country, and it is still far from fully studied. We need to continue its study in the aspect of creating improved resources for diagnosis and specific prevention. There are diseases about which we have simply forgotten, or in relation to which we think there is nothing left for science to do, that all problems have been solved.

A great amount of attention needs to be devoted to the problem of slow infections, both those which have long been known in the literature but which continue to be largely unstudied (scrapie, visna-maedi, adenomatosis, Aleut disease and encephalopathy in mink, arthritis-encephalitis in goats, Borna disease), and those which have recently appeared (spongiform encephalopathy in cattle) and may penetrate into our territory together with livestock or slaughterhouse products. The possibility is not excluded that we will encounter a similar situation in

application to cattle spongiform encephalopathy (the etiology of these diseases is the same, you see!). This disease has already been detected in cats and antelope in British zoos (A. Fleetwood, 1990; P. Aldhous, 1990).

Another task of epizootologists is to study diseases of wild animals. Little attention is being devoted to this for the moment. In the meantime links have long been discerned between the appearance and spread of infectious diseases in people and agricultural and domestic animals on one hand and morbidity of wild animals on the other. This link is clearly visible in regard to rabies. Study of diseases of marine mammals is also important. There have been interesting observations of vesicular exanthema in pigs, which become infected by it when given seal meat as food.

Die-offs of different species of marine animals (seals in the North Sea, seals in Lake Baikal etc.) are observed on the backdrop of excessive pollution of the oceans, seas and lakes by industrial wastes. Some scientists are prone to attribute these die-offs to viruses and other diseases, and particularly to carnivore plague. Incidentally, deeper research shows that we are dealing with a specific seal virus from the family Paramyxoviridae, which is antigenically kindred to carnivore plague virus. Cattle measles and plague viruses are known to belong to this group of viruses.

I believe that this seal virus has persisted in the bodies of seals for a long time, and that the disease has manifested itself only as a result of pollution of water basins; it is no accident that recently entire herds of marine mammals have been beached, since it is no longer possible to live in the water. [passage omitted].

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### **Listeriosis—A Dietary Infection (Danger, Indication Methods and Control Measures)**

927C0313B Moscow VETERINARIYA in Russian  
No 4, Apr 91 pp 32-36

[Article by I. A. Bakulov, V. M. Kotlyarov and T. I. Dushko, All-Union Scientific Research Institute of Veterinary Virology and Microbiology; UDC 619:616.981.136]

[Excerpt] [Passage omitted] As was already indicated, records have been kept on listeriosis in animals in our country since 1956. During these years it has been revealed in the most diverse geographic, natural and climatic zones. Animals of the RSFSR, Kazakhstan and the Ukraine are at the highest risk for this disease; sheep are infected most often, and cattle are in second place, followed by pigs.

According to V. A. Vedernikov, just in the RSFSR in 1988 listeriosis occupied second place among infectious diseases (15 nosological units) of cattle in terms of the



number of risk areas, third place in terms of the number of stricken animals, and second place in terms of the number of dead animals.

Unfortunately official registration of listeriosis in people has not been introduced in the USSR, although a large number of articles indicate that it is present in our country. Examples from one oblast are persuasive<sup>2</sup>. Using a large pig farm as an example, the authors demonstrated a direct dependence between occurrence of the disease in people and the degree of contact with agricultural animals. Our research (conducted jointly with specialists of the Moscow City Epidemiological Station and Nizhegorod University) revealed a case of listeriosis in a pregnant woman in 1989. It led to the death of her newborn infant (a pathogenic listeriosis strain was isolated from its body). The possibility that this woman was infected by rodents was demonstrated: She had lived in a rural area two months prior to giving birth.

These facts are confirmed by papers that have now become classics<sup>7-9</sup> communicating isolation of 83 strains of listeriosis in the Moscow area from gray rats, house and harvest mice, and bank and meadow voles (the research was conducted on 157,000 rodents). When over 20,000 animals from the rayons of Moscow Oblast were investigated, listeriosis was also isolated from bank voles, house mice and moles. According to the data of this author listeriosis is widespread throughout all of Moscow, but it is recorded more often on the outskirts than in the city center (infected animals were discovered more often in vegetable storehouses, livestock buildings, parks, gardens, residential buildings and trade and industrial facilities).

Listeriosis has been isolated from rodents in Kiev<sup>6</sup>, Zaporozhye<sup>10</sup>, Lugansk Oblast<sup>13</sup>, Khabarovsk<sup>4</sup>, Vladivostok<sup>5</sup>, Maritime and Khabarovsk krais, Chita and Kokchetav oblasts, Tuva ASSR and Buryat ASSR, and Irkutsk<sup>11,12</sup>. [passage omitted]

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### Chromosomal Aberrations in Peripheral Blood Lymphocytes in Inhabitants of Regions With Elevated Background Radiation

927C0245A Minsk DOKLADY AKADEMII NAUK BSSR in Russian Vol 35 No 8, Aug 91 (manuscript received 11 Feb 91) pp 745-748

[Article by N. P. Bochkov, K. A. Bedelbayeva, L. D. Katosova, and A. P. Ambrosyev, Radiobiology Institute, Belorussian SSR Academy of Sciences; All-Union Medical Genetics Research Center, USSR Academy of Medical Sciences, Moscow; UDC 575.244.23]

[Abstract] Cytogenetic examinations were performed in 1989-1990 for adults and children residing in areas contaminated by radiation from Chernobyl. The average density of cesium-137 ranged from 20-40 Ci/km<sup>2</sup>, while that of strontium-90 was 1.0-1.75 Ci/km<sup>2</sup>. At the Strelischevo Collective Farm, these figures were 17.0 Ci/km<sup>2</sup> for cesium-137 and 2.12 Ci/km<sup>2</sup> for strontium-90. Conventional methods were employed for classifying and counting all types of chromosomal aberrations that could be identified without karyotyping. Between 100 and 350 cells were analyzed from each person. The inhabitants of Vetka displayed a 3.04 +/- 0.16 percent aberration rate as opposed to 2.25 +/- 0.22 percent for the control group. The results demonstrated that most aberrant cells had one to two chromosomal aberrations. In addition, data on the cytogenetic screening of children revealed a much higher frequency of aberrant cells among those residing in contaminated areas. It was also shown that the peripheral blood lymphocytes in children are much more sensitive to radiation than those in adults. In conclusion, these findings demonstrate that people inhabiting regions polluted with radionuclides display a relatively higher frequency of chromosomal aberrations. Figures 1; tables 1; references 8: 7 Russian, 1 Western.

### Expression and Secretion of Human Growth Hormone in Methylophilic Yeast *Hansenula polymorpha*

927C0245B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 321 No 2, Nov 91 (manuscript received 06 Sep 91) pp 390-394

[Article by P. G. Aprikan, I. V. Karpychev, V. M. Mikhaylover, V. D. Gracheva, A. M. Shchedrin, M. Yu. Beburow, M. A. Eldarov, and K. G. Skryabin, Bioinzheneriya Engineering Center, USSR Academy of Sciences; Biotekhnologiya Scientific Production Association, Moscow; UDC 577.175.322.017.22:582.282.195.23]

[Abstract] The biosynthesis and secretion of human growth hormone (HGH) was investigated in recombinant strain *Hansenula polymorpha*, which bears the HGH gene under the control of promoter and terminator regions in the methanol oxidase gene of *H. polymorpha*. The recombinant plasmid DNA of pHPaH bearing HGH under the control of the methanol oxidase gene promoter and terminator was constructed based on plasmid pL3. The authors attempted to optimize the

conditions for cultivating the producer strain using methanol and glycerin as growth substrates that do not repress methanol oxidase gene transcription. The resultant transformants were cultivated on YPD/3 percent glycerin for 1-1.5 days, after which 1 percent methanol was added to the growing cultures. The results showed that this approach made it possible to increase the level of HGH secreted by more than an order of magnitude. In addition, the data demonstrated that the immunoreactive polypeptide secreted by *Hansenula polymorpha* corresponds to the mobility of mature hypophyseal HGH, but differs from the HGH secreted by *S. cerevisiae*. Furthermore, results of analyzing the condition of the pHPaH plasmid with Southern blot hybridization suggest that the pHPaH plasmid in the producer cells is in an integrated condition in the form of a single copy. In conclusion, a single copy of the integrated recombinant plasmid pHPaH is sufficient for a high level of expression and effective secretion of HGH. Figures 1; tables 1; references 15: 3 Russian, 12 Western.

### Cytogenetic Analysis of 1B Chromosome in Soft Wheat Somaculture With Altered Gliadin Component Composition

927C0246A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 320 No 5, Oct 91 (manuscript received 25 Jul 91) pp 1251-1253

[Article by S. A. Babayeva, A. K. Gaponenko, and T. F. Petrova, Bioinzheneriya Engineering Center, Molecular Biology Institute imeni V. A. Engelhardt, USSR Academy of Sciences, Moscow; UDC 575.224:633.111]

[Abstract] The correlation between mutability for gliadins, grain protein composition, and the structure of hexaploid wheat chromosomal regenerants was investigated with the use of dihaploid line AD 20/47 to produce callous lines of soft wheat. Conventional methods were employed for the callous induction of immature embryos, cultivation of somatic cells, regeneration, and further cultivation of plants. Grains from second generation regenerants were used for electrophoretic separation of gliadins. Embryonal rootlets from the grains were treated with a 0.2 percent colchicine solution for 1.5 hours and then 2°C water for 1.5 hours. Electrophoretic analysis of grain gliadins from SC<sub>2</sub> regenerant plants revealed somaclonal mutability characterized by a lack of or change in the intensity of individual components. In addition, differential staining of the metaphase plates revealed that the 1B chromosome bears a large amount of heterochromatin in the arm, which makes it possible to visually identify major chromosomal rearrangements. Furthermore, chromosomal rearrangements are more likely to occur in chromosomes with a large amount of heterochromatin. In conclusion, analysis of the correlation between mutability for the component composition of gliadins and the structure of somaclonal chromosomes showed that there were not any chromosomal rearrangements at the light level, probably as a result of aspects of gene expression and a change in expression with the

involvement of mobile elements and point mutations. References 15: 3 Russian, 12 Western.

### Healthy Tobacco Plants Bear Nucleic Acid Molecules Related to Tobacco Mosaic Virus

927C0246B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 320 No 5, Oct 91 (manuscript received 31 Jul 91) pp 1254-1257

[Article by S. P. Smirnov and V. A. Pukhalskiy, General Genetics Institute imeni N. I. Vavilov, USSR Academy of Sciences, Moscow; UDC 575]

[Abstract] This paper presents data suggesting the presence of virus-related molecules of nucleic acids in healthy tobacco plants. Two weeks after healthy tobacco plants grown under normal and aseptic conditions were infected, the authors noted a considerable increase in the amount of tobacco mosaic virus (TMV)-related molecules of nucleic acids. The results of studies with cucumber mosaic virus (CMV) suggest that tobacco plants synthesize nucleic acid molecules homologous to genomic TMV RNA, the amount of which sharply increases in plant cells following infection with TMV, but remains unaltered when infected with CMV, which is unrelated to TMV. Hybridization experiments with several probes showed that TMV-related molecules of nucleic acids include sequences homologous to the 5' and 3' terminal sections of TMV RNA. Hybridization of nucleic acids isolated from healthy tobacco plants produced two hybridization signals of 1,000 and 200 nucleotide pairs. Additional research on these signals revealed that the 1,000 np signal was most likely double-stranded RNA, while the 200 np signal was more typical of DNA. Accordingly, these data suggest that healthy tobacco plants bear molecules related to TMV and that these molecules are homologous to the terminal sequences of TMV RNA. However, the mechanism by which these molecules are synthesized remains vague. In conclusion, these data suggest that nucleotide sequences can be exchanged between viruses and plants. Figures 2; references 10: 3 Russian, 7 Western.

### Cloning and Description of Human Genome Locus Bearing Gene for Second Type of Receptor (75 kD) for Tumor Necrosis Factor and Lymphotoxin

927C0246C Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 320 No 5, Oct 91 (manuscript received 07 Aug 91) pp 1258-1261

[Article by R. L. Turetskaya, I. A. Udalova, D. V. Kuprash, A. V. Terskikh, and S. A. Nedospasov, Molecular Biology Institute imeni V. A. Engelgardt, USSR Academy of Sciences, Moscow; UDC 577.212.3]

[Abstract] The objective of this investigation was to clone and describe the human genome locus bearing a chromosomal copy of the gene that codes for a tumor necrosis factor (TNF) receptor with a mass of 75 kD.

Three recombinant clones bearing human cDNA insertions with an average size of 17,000 np were isolated, one of which hybridized with two probes. A physical map of the cloned section of the human genome was constructed by cleaving the DNA with combinations of restriction endonucleases and Southern hybridization with probes. The results demonstrated that recombinant clones 2, 3, 6a, and 11 isolated from the human genome clone library together bear the complete chromosomal copy of the human gene that codes for the second type of receptor for TNF and lymphotoxin (a polypeptide with an apparent molecular mass of 75 kD). Mapping of the positions of potentially polymorphic microsatellites revealed genetic polymorphism in the human genes coding for TNF and lymphotoxin. Moreover, more than 30 neutral alleles of this genome locus were identified. In addition, hybridization of short synthetic oligonucleotides revealed that there is one AC type microsatellite in the entire genome locus located in one of the introns in the gene approximately 2,000 np from the beginning. Figures 2; tables 2; references 15: 1 Russian, 14 Western.

### Development of Bifunctional Derivatives of Gene From Insectotoxin *Bacillus thuringiensis* Var. *Kurstaki* for Expression in Transgenic Plants

927C0247E Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 321 No 2, Nov 91 (manuscript received 21 Aug 91) pp 412-415

[Article by Ye. V. Kuzmin, A. A. Shadenkov, S. V. Uzbekova, and M. F. Shemyakin, All-Union Scientific Research Institute of Agricultural Biotechnology, All-Union Academy of Agricultural Sciences imeni V. I. Lenin, Moscow; UDC 577.1]

[Abstract] The objective of this investigation was to construct derivatives of an insectotoxin gene from *Bacillus thuringiensis* var. *kurstaki* HD1 (specific for lepidopterans) that would code for proteins with both insecticidal activity and kanamycin phosphotransferase or  $\beta$ -glucuronidase activity. In addition, it would also need to be capable of normal expression in plants. The NsiI-KpnI fragment from plasmid pOC2 (donor for insectotoxin gene from *kurstaki* HD1) contains the complete coding sequence of the toxic domain. It was subcloned into plasmid pUC19S so that the insectotoxin coding sequence preceded the 19S promoter and 32 5' end triplets of gene VI from cauliflower mosaic virus. Data from electrophoresis and immunoblotting revealed that *Escherichia coli* synthesizes immunoreactive polypeptides with molecular masses of 70, 90, and 155 kD. The comparative insecticidal activity of the recombinant proteins, products of plasmids pTrctt, pTrctn, and pTrctg was determined by means of a biotest on *Lymantria dispar* silkworm caterpillars. The results demonstrated that the biological activity of the insectotoxin-glucuronidase hybrid was much lower than that of the insectotoxin-kanamycin phosphotransferase hybrid, probably due to an upset in the proteolytic processing of this protein in the insect intestine. These results confirm

data from other studies showing an insectotoxin-kanamycin phosphotransferase bifunctional protein can be produced. In conclusion, the findings also suggest that other bifunctional proteins can be constructed with other reporter activities. Figures 2; references 9: 3 Russian, 6 Western.

**Interaction of *Escherichia coli* and *Francisella tularensis* RNA Polymerase With Hybrid Plasmids Bearing Fragments of Chromosomal DNA From *Francisella tularensis***

927C0299A Moscow MOLEKULARNAYA  
GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA  
in Russian No 7, Jul 91 (manuscript received 11 Jun 90)  
pp 12-15

[Article by A. P. Pomerantsev, I. V. Domaradskiy, I. P. Doronin, and Yu. V. Yershov, All-Union Scientific Research Institute of Applied Microbiology, Obolensk, Moscow Oblast; UDC 579.841.95:579.25:577.214]

[Abstract] The objectives of this investigation were to clone promoter-bearing fragments of cDNA from *Francisella tularensis* in *Escherichia coli* cells, evaluate the effectiveness of regulating gene expression with these promoters in homologous and heterologous systems, and determine the frequency of binding of RNA polymerase from *F. tularensis* and *E. coli* with plasmids bearing cloned fragments of cDNA from a tularemia microbe. The vector pSK was employed to clone promoter-bearing fragments of cDNA from the tularemia microbe. Restriction analysis of the plasmids isolated from both microorganisms demonstrated that the plasmids in *F. tularensis* and *E. coli* were identical. The results showed that four groups of plasmids were obtained, some of which expressed the Tc<sup>R</sup> phenotype and the tet-gene. Comparison of the effectiveness of binding *E. coli* RNA polymerase with *F. tularensis* fragments as opposed to the vector demonstrated that effectiveness frequently is much higher than for the vector section. The high effectiveness of the binding of *E. coli* RNA polymerase with fragments of *F. tularensis* cDNA is attributed to negative deviation from ideal behavior during investigation of the transcription of *E. coli* RNA polymerase from the binary system of *E. coli*-*F. tularensis* DNA. The lack of expression of the tet-gene in *E. coli* cells is apparently due to the absence of a preferred binding site for *E. coli* RNA polymerase in the vicinity of its promoter. Figures 4; references 11: 4 Russian, 7 Western.

**Investigation of Biochemical, Antigenic, and Protective Properties of External Membrane of Tularemia Etiological Agent**

927C0299B Moscow MOLEKULARNAYA  
GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA  
in Russian No 7, Jul 91 (manuscript received  
10 Aug 90) pp 15-20

[Article by V. S. Khlebnikov, I. R. Golovlev, D. P. Kulevatskiy, S. F. Averin, S. Yu. Pshirkov, N. V. Tokhtamysheva, V. Ye. Zhemchugov, L. A. Safonova, V. N. Gerasimov, A. M. Chugunov, S. S. Vetchinin, V. G. Galaktionov,

and S. S. Afanasyev, Immunology Institute, Ministry of the Medical Industry, Lyubuchany, Chekhovskiy Rayon, Moscow Oblast; All-Union Scientific Research Institute of Applied Microbiology, Obolensk, Moscow Oblast; UDC 579.841.95:579.222]:579.232]

[Abstract] The objective of this study was to investigate the morphological, biochemical, and antigenic characteristics of the external membranes of *Francisella tularensis* and determine their protective properties under native conditions and when combined with chitosan. Electron microscopy data revealed round and irregular electron transparent structures with a three-layer profile in ultrathin sections. Investigation of the lipopolysaccharide preparations in a diffusion precipitation reaction in agarose gel with the use of monoclonal antibodies showed that FB11-x monoclonal antibodies form precipitates with lipopolysaccharides. Subsequent immunoblotting of the lipopolysaccharides with the use of FB11-x monoclonal antibodies on nitrocellulose replicas revealed all lipopolysaccharide bands, with two exceptions. Investigation of the lipopolysaccharide protective properties showed that preparations isolated from external membranes and acetone-dried cells do not protect CBA mice from death following infection with virulent strain 503 of tularemia. The next stage of the investigation was to determine the protective properties of external membranes in native form as well as when combined with the immunostimulant chitosan. Chitosan is a homopolysaccharide, molecular mass 120 kD, that can stimulate primary and secondary immune responses. CBA mice were immunized once with an external membrane preparation (8- 1000 µg) or mixtures of external membranes and chitosan (25-100 µg) given in subcutaneous or intraperitoneal injections. The mice were then infected 21 days later with two-day cultures of tularemia (70 live microbial cells) again given in subcutaneous or intraperitoneal injections. The results demonstrated that a single immunization with the external membrane preparation protects mice from infection with tularemia strain 503. In addition, it was shown that the ED<sub>50</sub> of the external membrane preparation was four times lower when administered intraperitoneally than when given subcutaneously. Furthermore, the data demonstrated that adding chitosan to the external membrane preparation in a dose of 25 µg enhances their protective properties in intraperitoneal immunization. Figures 5; tables 2; references 24: 7 Russian, 14 Western.

**Sensitizing Properties of Brucella Protein Antigens Produced in *Escherichia coli* K12 Cells**

927C0299C Moscow MOLEKULARNAYA  
GENETIKA, MIKROBIOLOGIYA I VIRUSOLOGIYA  
in Russian No 7, Jul 91 (manuscript received 17 Oct 90)  
pp 29-32

[Article by V. Ye. Malikov, D. F. Selyutina, V. N. Gorelov, V. A. Chibisova, and Ye. A. Dranovskaya, Epidemiology and Microbiology Scientific Research Institute imeni N. F.

Gamaleya, USSR Academy of Medical Sciences, Moscow;  
UDC 579.841.95:579.222:547.96]:579.61:[616-  
092:612.017.2]

[Abstract] Comparative investigation of the sensitizing properties of brucella protein antigens with molecular masses of 31 and 31+15 kD produced in *Escherichia coli* cells and containing protein preparations isolated from brucella cell walls was performed using groups of animals immunized with brucella protein antigen preparations in a dose of 100 µg. The data showed that both protein preparations display sensitizing properties, but the 31 kD protein preparation is more likely to form delayed hypersensitivity. Use of a test of edema of the paws in mice made it possible to also reveal the ability of the brucellosis chemical vaccine to form delayed hypersensitivity. This, however, is less pronounced than that with bacteria cells, the protein antigen, and the 31 kD protein preparation. The results demonstrated that brucella lipopolysaccharides (10 µg) and *E. coli*

lipopolysaccharide (1 µg) preparations caused the deaths of all experimental animals treated with actinomycin D in the first 24 hours, while protein preparations in a dose of 100 µg reduced the number of deaths to only 30 percent of the animals within 7 days. Edema in the mice immunized with the 31 kD protein preparation and a preparation of *E. coli* antigens was 19.8 µg as opposed to 16.8 µg in the control group. These results suggest that the 31 kD protein preparation does not contain any components of the *E. coli* K12 antigenic structure that can evoke a condition of delayed hypersensitivity which can be detected by homologous antigens. The data also indicated that this test is most informative in the diagnosis of chronic forms of brucellosis when serological results are negative and clinical signs have disappeared. In conclusion, the protein antigen with a molecular mass of 31 kD is a promising preparation for the allergodiagnosis of brucellosis in reactions both *in vivo* and *in vitro*. Figures 3; references 24: 11 Russian, 13 Western.

### Monoclonal Antibodies to Human Small Cell Lung Cancer

927C0292A Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY  
in Russian Vol 112 No 9, Sep 91 (manuscript received  
05 Oct 90) pp 282-285

[Article by M. A. Goncharskaya, N. M. Rutkevich, A. G. Tonevitskiy, N. F. Orel, A. V. Vasilyev, N. I. Perevodchikova, and Ye. B. Mechetner, Immunochemistry Laboratory, Carcinogenesis Scientific Research Institute, All-Union Cancer Science Center, USSR Academy of Medical Sciences; Cellular Immunology Group, Experimental Cardiology Institute, All-Union Cardiology Research Center, USSR Academy of Medical Sciences, Moscow; UDC 616.24-006.6-078.3-092.9]

[Abstract] The objective of this investigation was to produce and describe monoclonal antibodies to human small cell lung cancer (HSCLC) for possible use in immunodiagnosis and immunotoxin synthesis. The mice were immunized intraperitoneally with H417 cells (HSCLC). Splenocytes from immune mice were hybridized with murine myeloma SP2 cells. The authors obtained 38 clones that positively reacted with H417 cells. Indirect immunofluorescence was then employed to select five primary clones that did not react with normal bone marrow cells and did react with tumor preparations. Immunoblotting was used to determine the specificity of antibodies to the cell surface protein antigens of H417 cells. The results suggest that these antibodies may be used for the immunodiagnosis of SCLC metastases in bone marrow, but because of a cross reaction, they cannot be used for the effective differential diagnosis of small cell and non-small cell lung cancers. Figures 3; tables 1; references 13: 2 Russian, 11 Western.

### Use of Liposomes for Associating Foreign Genetic Material With Sperm Cells

927C0292B Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY  
in Russian Vol 112 No 9, Sep 91 (manuscript received  
28 Jan 91) pp 292-293

[Article by A. V. Gorlova and V. P. Torchilin, Experimental Cardiology Institute, All-Union Cardiology Research Center, USSR Academy of Medical Sciences, Moscow; UDC 612.616.2+547.963.32.915.5]

[Abstract] The objective of this investigation was to select the optimal liposome composition for inclusion in their DNA and absorption in sperm cells as well as to assess the functional activity of sperm cells modified by liposomes. Experiments with radioactively labeled DNA revealed that tristearoxypropylenediol-1-0-phosphohomocholine (PHC):1,2-di-oleoyl-sn-glycero-3-phosphoethanolamine (DOPE) liposomes incorporated 80 percent of the labeled DNA, while 1,2-diacyl-sn-glycero-3-phosphocholine liposomes incorporated only 20 percent. These data and data from

calcein dye experiments indicated that the PHC and distearoxy-ethylenediol-1-0-tion-phosphohomocholine incorporated the two markers two to four times better than the control liposomes. Following incubation, visual analysis of sperm cell functional activity using a ten-point scale revealed that the sperm cells agglutinate in lipid concentrations exceeding 300 ng per million cells, but that at lower concentrations the sperm are more active and no agglutination occurs. Tables 4; references 7: 4 Russian, 3 Western.

### Morphofunctional Investigation of Experimental Staphylococcus and Pyocyanic Infections in Rats Against Background of Administration of Dalargin, Synthetic Analog of Endogenous Opioids

927C0292D Moscow BYULLETEN

EKSPERIMENTALNOY BIOLOGII I MEDITSINY  
in Russian Vol 112 No 9, Sep 91 (manuscript received  
06 Nov 91 [as published]) pp 317-321

[Article by S. B. Pashutin, R. I. Kayem, and T. D. Zinov'yeva, Surgery Institute imeni A. V. Vishnevskiy, USSR Academy of Medical Sciences, Moscow; UDC 616.98:579.861.2]+616.98:579.841.11]-085.31:[547.95:647.943]

[Abstract] The objective of this study was the morphofunctional investigation of the status of the primary focus and parenchymal organs in 104 male Wistar rats (250-270 g) during an experimental generalized infection induced by *Staphylococcus aureus* (strain 6567) and *Pseudomonas aeruginosa* (strain 487). The animals were infected with either the gram-positive or gram-negative microorganisms in a dose of  $10^{12}$  cells by means of an intramuscular injection into the right thigh. Dalargin in a dose of 100 µg/kg was injected into the left thigh six and 18 hours, and one, two, and three days after infection. The extent of the infection process was assessed by both the survival rate of the animals and the results of bacteriological investigation. The findings revealed that the course of both infections was quite similar, although with *P. aeruginosa* the alterations and visible signs of local reaction were more pronounced. The infection with gram-negative microflora displayed a lower level of generalization, indicating that *P. aeruginosa* has an effect similar to that of *S. aureus*, but with a lower concentration of bacteria. In addition, with *P. aeruginosa* the destructive processes in the wound were more extensive. These results suggest that the low pathogenicity of *P. aeruginosa* is due to a certain level of adaptation by the etiological agent. The authors observed an increase in resistance to infection in experimental rats against the background of exogenous administration of the regulatory peptide dalargin. It was shown that the effectiveness of the preparation is largely determined by the type of bacteria. Dalargin reduces the mortality rate with gram-positive bacteria to 10 percent, while the rate is 30 percent for gram-negative bacteria. With respect to this investigation, the protective effect of



dalargin is attributed to a decrease in hormonal-metabolic upsets and several rheological disturbances as well as improved microcirculation and an increase in the processes of reparative regeneration of damaged tissues. It was also noted that the pathomorphosis of an infection treated with dalargin is marked by a decrease in the scale of destruction, limited area of damage, and a decrease in vascular disturbances. In conclusion, the combination of a number of properties inherent to opioid peptides makes possible the effect of enkephalins on the pathogenesis of a purulent infection, which results in increased effectiveness of pathogenetic therapy in the comprehensive treatment of different types of purulent-septic complications stemming from surgery. Figures 2; tables 1; references 14 (Russian).

### Effect of Met-Enkephalin on Blast Transformation of Splenocytes in Mice

927C0317 Moscow IMMUNOLOGIYA in Russian  
No 4, Apr 91 (manuscript received 9 Oct 90) pp 24-25

[Article by L. A. Kheday, B. B. Kim, S. V. Zaytsev, Ye. M. Gavrilova, L. A. Zakharova, and A. A. Mikhaylov, Moscow State University imeni M. V. Lomonosov; Institute of Bioorganic Chemistry, USSR Academy of Sciences; UDC 615.31:547.95:547.943].015.4:[612.441.014:576.36].07]

[Abstract] Stress that causes opioid-mediated analgesia can suppress PHA- and ConA-induced proliferation of lymphocytes. Although the participation of the  $\beta$ -endorphin in those processes is rather clear, the role of the N-terminal pentapeptide—met-enkephalin (ME)—is not. That is, in vivo experiments have shown the introduction of ME in mice to strengthen the mitogenic response of splenocytes to PHA, whereas in vitro experiments have failed to demonstrate any effect on ConA- or PHA-induced blast transformation or on IL-2 production by mouse splenocytes stimulated by ConA. The researchers here chose to study the effect of ME on blast transformation induced by staphylococcal enterotoxin A and ConA in mouse splenocytes. The experimental animals consisted of (CBA X C57BL/6)F<sub>1</sub> mice. ME was found to suppress ConA-induced splenocyte proliferation, with a maximum effect at  $10^{-9}$  M. It activated enterotoxin-A-induced proliferation via blast transformation in a concentration range of  $10^{-8}$ - $10^{-14}$  M, with modulation amplitude higher for mice with a high pain threshold (47-58 s). The opioid-receptor antagonist nalaxone, in a concentration of  $5 \times 10^{-7}$  M, cancelled the effect in the enterotoxin-A-induced proliferation. Figures 3, references 7; Western.

### Study of the Effect of Chlororganic and Phosphororganic Compounds on E Production in Experiment and in Immunoepidemiological Research

927C0317B Moscow IMMUNOLOGIYA in Russian  
No 4, Apr 91 (manuscript received 14 Dec 90) pp 31-34

[Article by A. A. Polner, A. A. Vlasov, M. Yu. Syusyukin, M. Z. Saidov, N. M. Golubeva, Institute of Immunology, USSR Ministry of Health, Moscow; UDC 616. 153.962.4-097-092.9-078.33]

[Abstract] Both long-term and short-term use of agricultural and household insecticides and pesticides containing chlororganic and phosphororganic compounds can lead to secondary immune deficiencies that have been well studied over the years, i.e., drop in T and B lymphocytes, inversion of the CD4<sup>+</sup>/CD8<sup>+</sup> ratio, and dysimmunoglobulinemia. The body's shift toward the allergic component, however, has been little studied, a fact that prompted the researchers here to look at the E response in (CBA X C57BL/6)F<sub>1</sub> mice injected three times intraperitoneally with 5  $\mu$ g/mouse recrystallized ovalbumin adsorbed on 5 mg/mouse aluminum hydroxide. Secondary response was induced by injection of the same dose of antigen one week later. Chlororganic and phosphororganic compounds—trichlorophenol (TCP), chlorphenoxipinocholine (CPCh), diesteroheterophosphate (DEHP), and glyphosphate (GP)—were injected intraperitoneally along with the antigen. E serum levels dropped within seven days after injection of TCP (0.1-100  $\mu$ g/mouse), as did E development by bone marrow cells. Spleen and lymph node production of E was not affected. Injection of 0.5 percent and 2 percent concentrations of CPCh lowered serum E and suppressed E development by spleen, lymph nodes, and bone marrow. DEHP suppressed E response in concentrations of more than 2 percent. GP, in various concentrations ranging from 1 percent to 20 percent, had varying effects on bone marrow, suppressing its production of IgE at the lower end of the concentration continuum, but enhancing it at the upper end. Comparative retrospective studies of individuals employed at the Shchelkovo Experimental Plant, which produces the compounds under study, mirrored the experimental data, with individuals who had worked at the plant longest exhibiting hyperproduction of E rather than hypoproduction. Figures 2, references 13: 7 Russian, 6 Western.

### New Approach to Evaluation of Dose of Immune-Correcting Myeloid Preparation

927C0317C Moscow IMMUNOLOGIYA in Russian  
No 4, Apr 91 (manuscript received 13 Dec 90) pp 67-68

[Article by S. Yu. Shanurin, O. G. Yanovskiy, Ye. A. Kirilina, and A. A. Mikhaylov, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow; UDC 615.275.4.015.3.07]

[Abstract] In the production of myeloid, the absolute content of the active substances in the highly pure fraction isolated from the supernatant is virtually impossible to measure, primarily because myelo-peptides are biologically active in extremely low concentrations. The Lowry method of determining protein content does not provide a true picture of the content bioactive material. The method proposed here for estimating myeloid dose is based on level of biological activity and regards the capacity of the preparation to stimulate antibody formation at the peak of immune response as an integral indicator of activity. Preliminary experiments established that the peak of antibody formation in response to bovine  $\gamma$ -globulin injected in (CBA X C57BL/6)F<sub>1</sub> mice was on the fifth day of secondary immune response, one day after the mice were sacrificed. The mice had been initially immunized IM with the  $\gamma$ -globulin in total



Freund's adjuvant in a dose of 100 µg/mouse, which was followed three weeks later without the adjuvant. Various production series of the myeloid were studied in the experiment. The researchers found a direct linear correlation between number of cells and optical density, with a linear regression equation taking the form  $y = -0.77 \pm 0.00192x$ , where  $x$  is the number of cells in culture and  $y$  is the optical

density. Addition of myeloid on the fourth day after secondary immune response led to a dose-dependent stimulation in antibody formation in the productive phase of the secondary immune response. Regression analysis revealed no consistent differences for the coefficients of the linear regression equations for the various myeloid series, indicating similar compositions. References 2: Russian.

**Immunostimulating Effect of Microwaves and UHF Electrical Field on Systemic Lupus Erythematosus Patients**

927C0197C Moscow *VOPROSY KURORTOLOGII, FIZIOTERAPII I LECHEBNOY FIZICHESKOY KULTURY* in Russian No 4, Jul-Aug 91 (manuscript received 26 Feb 91) pp 36-40

[Article by V. D. Sidorov, S. B. Pershin, A. S. Bobkova, and A. I. Galenchik, All-Union Medical Rehabilitation and Physical Therapy Research Center, Moscow; UDC 615.849.112.03:616.5-002.525.2-031.81]-015.4:612.017.1]

[Abstract] The immunostimulating effect of bitemporal UHF and decimeter wave therapy on the adrenal glands was investigated in 62 chronic systemic lupus erythematosus female patients aged 21-50 who had suffered from the disease for three to 12 years. Group one was exposed to decimeter waves at the adrenal glands with 30-35 W. Group two was exposed to a UHF electrical field using a bitemporal method with 30-35 W. The courses consisted of 18-20 daily treatments. All subjects were also given five to 15 mg/day prednisolone. In addition, the patients were administered one of the following: plakvenil [sic] (0.2 g/day), cyclophosphamide (0.05 g/day), azathioprine (0.05 g/day), or delagil (0.25 g/day). Significant improvement in the form of complete disappearance of polyarthralgia, myalgia, and painful contractures was noted in 27 percent of group one, and in 66 percent of group two. Respectively, 35 percent and 23 percent noted less pain. These findings suggest that the greatest therapeutic impact was reached in group two as a result of the effect of the UHF electrical field on the hypothalamus and hypophysis. Conversely, decimeter waves focused directly on the adrenal glands were less effective. The UHF electrical field is used as a pathogenetically based remedy of choice on the higher centers of neuroendocrine regulation. Accordingly, bitemporal UHF therapy is marked by the possibility of selecting the effect for organ or tissue while preventing a wide array of drug effects inherent to drug therapy. Tables 2; references 7: 6 Russian, 1 Western.

**Neurotrophic Effect of Endogenous Peptides Exhibiting Therapeutic Effect in Parkinson's Patients**

927C0247A Moscow *DOKLADY AKADEMII NAUK SSSR* in Russian Vol 321 No 1, Nov 91 (manuscript received 26 Aug 91) pp 198-202

[Article by S. A. Dambinova, M. V. Kozlova, Yu. V. Bobryshev, G. V. Konovalov, V. U. Kalenchuk, N. G. Slepko, O. N. Koresheonkov, and K. A. Shevchenko, Human Brain Institute, USSR Academy of Sciences, St. Petersburg; Experimental Cardiology Scientific Research Institute, All-Union Cardiology Research Center, USSR Academy of Medical Sciences, Moscow; Military Medicine Academy, St. Petersburg; UDC 611-018.8:577.122:611.858-008.6]

[Abstract] The possible neurotrophic properties of low molecular weight (less than 2.5 kD) endogenous peptides

were investigated to determine the mechanism of their positive clinical effect on Parkinson's disease patients. Peptide fractions were obtained from organotypical cultures of the spinal cord from day-old Wistar rat embryos. Preliminary results indicated that these peptide fractions normalize the mediator metabolism in the cerebrospinal fluid that has been upset in Parkinson's patients. Peptide fraction 2/2 obtained after high performance liquid chromatography displayed a positive clinical effect in the form of a dramatic improvement in motor function that could be correlated with a change in the catecholamine level in the cerebrospinal fluid. It was also shown that adding this fraction to a growth culture considerably enhanced the intensity of culture growth. Peptide fraction 1/1 displayed a lesser therapeutic effect than fraction 2/2. Morphological analysis of rat spinal cord cultures revealed three zones: central zone, growth zone, and transitional zone. This illustration of the neurotrophic effect of these fractions in models of nerve tissue culture agree well with results obtained on the effect of opioid peptides and substance P and confirm that the peptides may increase the viability of neurons. The persistent positive impact of these peptide fractions is mediated through the processes of neuronal cell differentiation. In conclusion, further investigation of the biological activity of these peptides will reveal new perspectives in the development of a non-traditional class of drugs for treating motor disorders. Figures 2; tables 1; references 15: 8 Russian, 7 Western.

**New Treatment Removes Toxic Substances**

927C0265B Moscow *VECHERNYAYA MOSKVA* in Russian 16 Jan 92 p 5

[Article by Yu. Levin, professor, director of All-Union Center of Clinical Lymphology, from notes by Boris Samoylov, "AIDS-II: Ecology Within Us"]

[Text] Our society is tormented by a host of problems: political, national, economic, nutritional...but among them is one that may be more important than all the rest, for it determines the time of our physical existence. Not many know that an ecological disaster is developing inside of each of us.

We behave like madmen, involuntary accomplices to mass suicide, blankly staring at the degeneration and extinction of our friends and children. How else can one understand that while totally giving ourselves up to what would seem to be ambitious tasks, though special to our own existence, we have still not recognized that we are sick with endoecological disease, almost to a man. It makes us invalids, destroys, makes all else meaningless. The fact is that the epicenter of the ecological crisis long ago moved from the outer to the inner environment. Dozens of poisonous "bombs" that have penetrated or been formed in the organism are continuously exploding our cells, organs and tissues.

Here are a few figures. Only 23 percent of children remain healthy by the age of seven years, and only 14 percent by age seventeen. Almost half of the youth of military age are unfit to serve in the army according to their state of health; there is more: Since the seventies, there has been a rise in the frequency of ecologically dependent illnesses—cardiovascular and oncological. In general, an endoecological epidemic is gathering tornadoic speed, leaving no hope for the ancient Russian “something might turn up.” Something will have to be done.

What is it specifically that causes endoecological disease? The answer to this question is known. Endoecological poisonings are caused by microdoses of numerous toxic agents, sometimes not even exceeding the threshold of sensitivity. However, the effect of one poison is intensified by the action of another. They become partners in crime. Upon penetrating into the organism with polluted air, low-quality food and water, foreign substances are spread by the blood to organs and tissues. They are partly held there and become an initiating mechanism of self-poisoning.

This ailment is associated not only with the action of toxins on the organism, but also with the incapacity of systems of internal protection to render them harmless. Like AIDS, endoecological disease may run for a time without pronounced symptoms. People catch colds more often, and suffer from infectious, allergic and other ailments. The organism gradually and increasingly loses its capability of resistance to pathogenic factors, and a person may die of a “trivial” ailment.

Amazing but true, ecopoisonings are like an inherited disease. If parents have had it, their children will be affected.

Recently, workers at our center in the course of their research determined the makeup of chemical elements in the blood of practically healthy residents of Moscow and Podmoskovye. These elements are not poisons. However, their concentration in air and water has been increasing in recent years; we decided to check out how this has been reflected in the health of people. We learned that the level of many elements has increased inside of us as well, and this is already not totally safe. People with an elevated content of “normal” substances cannot be considered healthy. This is yet another symptom of endoecological disease.

We have come up with an original idea for dealing with ecopoisonings: cleaning the organism by stimulating the motion of water in organs and tissues. An artificially intensified stream of water can completely flush out harmful substances and poisons.

The human body is three fourths water. It runs in a continuous stream with dissolved substances through the walls of capillaries into the intercellular tissue and cells, yielding up these substances and picking up spent material, ever repeating its nutritive and cleaning cycle; here is the paradox: Among the mass of drugs, agents and

methods of treatment, there have been none that intensify the cleansing transport of water. Medical science has been stalled in this area for decades.

First of all, it has been necessary to determine whether artificial intensification of the movement of liquid would flush out toxins from the tissues without doing harm to the patient. We were afraid that the intensified stream of water might wash out and carry off useful materials along with harmful substances, thereby producing a destructive effect. A light shower merely lays the dust, while a downpour washes everything away.

In experiments on animals, and then in studies on people, it was learned that the process of water movement in organs and tissues can be regulated by drugs. This can be accomplished by prepared medicines, medicinal herbs and plants, lasers and ultrasonics. For example, we have used mannitol. This drug has previously been used for kidney diseases, hydrocephaly and other illnesses. It has been found that the drug readily displaces water from the space between cells.

The new form of treatment has been most effective in treating myocardial infarction. Infarction results from disruption of blood flow to some section of the heart. Heart cells die when deprived of nutrition. These are surrounded by working healthy cells, which are normally supplied with nutriment. But they are healthy only as long as the decaying dead cells do not poison the space surrounding them and the nearby live cells. This is where the myocardial flushing method developed by our team is of assistance. Drugs discovered for this purpose intensify the flow of water that flushes and cleans the habitat of living cells. Use of the new method has already saved many lives.

The surgical method that we have invented has come into wide use. It helps to clean the internal environment of the organism in case of severe inflammations, and speeds up healing of wounds. We ourselves are now helping victims of Chernobyl to rid themselves of contamination by radioactive substances, are treating patients suffering from bronchial asthma and vascular ailments.

A few words about prospective areas of research. It is known that emotional stress also disturbs metabolism. Until now, no one has removed from the tissues the toxins that arise as a result of mental stress. We will try to do this.

#### **Serum Glycoamines of BALB/C Mice and Aggregation of Experimental Rhabdomyosarcoma Cells**

927C0296A Kiev EKSPERIMENTALNAYA  
ONKOLOGIYA in Russian Vol 13 No 6, Nov-Dec 91  
(manuscript received 27 May 91) pp 27-33

[Article by M. D. Linetskiy, R. A. Semenova-Kobzar and G. V. Glinskiy, Institute for Oncology and Radiobiology Problems imeni R. Ye. Kavetskiy, Ukrainian SSR Academy of Sciences, Kiev; UDC 616.33-006.6:576.524:547.9]

[Abstract] An analysis was conducted on the impact of low MW ( $< 10$  KD) serum fractions of two to three month old female BALB/c mice bearing transplantable rhabdomyosarcoma on adhesiveness of the malignant cells. The results confirmed previous observations that both the  $< 10$  KD fraction and glycoamines isolated from this fraction by liquid chromatography inhibited in vitro aggregation. In addition, in vivo pulmonary metastatic potential of transplantable tumor cells preincubated with the glycoamines was markedly reduced. The effects of the glycoamines were attributed to galactose residues which reacted with lectin-like endogenous substances on the neoplastic cells. If further confirmation of this observation is provided, it would suggest that endogenous factors influence specific intercellular interactions of malignant cells and thereby modulate their invasiveness. Figures 8; references 18: 4 Russian, 14 Western.

**Immunomodulation of Pliss Lymphosarcoma in Rats by Hemoperfusion on Immunosorbent**

927C0296B Kiev EKSPERIMENTALNAYA  
ONKOLOGIYA in Russian Vol 13 No 6, Nov-Dec 91  
(manuscript received 12 Apr 91) pp 61-63

[Article by A. V. Sobko, Institute for Oncology and Radiobiology Problems imeni R. Ye. Kavetskiy, Ukrainian SSR Academy of Sciences, Kiev; UDC 616-006-092.9:615.246.9]

[Abstract] Outbred male rats, 350-400 g, bearing Pliss lymphosarcoma were used in a study to further define the therapeutic effects of hemoperfusion over an adsorbent bed consisting of killed *Staphylococcus aureus* Cowan 1 coupled to activated charcoal fibers. The results showed that one course of hemoperfusion equivalent to 50 percent of the circulating blood volume over a 200 mg adsorbent increased the survival rate to a mean of 31.1 days, vs. a 23.1 day survival figure for control rats. Additional studies demonstrated that cytotoxic activity of mononuclear cells against the Pliss cells was not affected by this procedure. Accordingly, the beneficial

effects of hemoperfusion were attributed to partial elimination of blocking factors which attenuate cellular immunity against neoplastic cells. Figures 2; tables 1; references 11: 4 Russian, 7 Western.

**Use of Chlotazol as Immunomodulating Agent in Chronic Bronchitis**

927C0320 Moscow KLINICHESKAYA MEDITSINA  
in Russian Vol 69 No 4, Apr 91 (manuscript received  
22 Jan 91) pp 58-60

[Article by A. I. Kleyner, L. M. Shmuter, V. M. Makotchenko, V. A. Yefremova, Ya. I. Khodzhay, and V. S. Trukh, Kharkov Scientific Research Institute of Labor Hygiene and Occupational Diseases, Ukrainian Institute of Postgraduate Medicine; UDC 616.233-002.2-085.275.4-036.8]

[Abstract] Based on the fact that chlotazol—a new, low-toxicity, nonsteroid antiinflammatory agent used as an antimicrobial, fever-reducing agent—has been shown to have a positive effect on immune status, the researchers here studied its immunomodulating action in three groups of individuals with chronic obstructive bronchitis. The efficacy of chlotazol, combined with routine therapy for bronchitis, was tested against routine therapy alone and routine therapy accompanied by treatment involving sodium nucleic acid. Chlotazol was found to be as effective as sodium nucleic acid in terms of immunomodulating action, although it demonstrated a more pronounced capacity for bringing T-system immune indicators (erythrocytes, absolute number of T-lymphocytes, theophylline-sensitive T-lymphocytes) back to baseline than did sodium nucleic acid. The latter agent demonstrated a more pronounced effect on the B-system indicators. The researchers recommended the new agent's use for chronic bronchitis in combination with routine therapy consisting of the administration of expectorants and broncholytics, oxygenotherapy, respiratory exercises, and, if necessary, antibacterial agents. References 14: Russian.

### Quick Method of Identifying Mycobacteria

927C0313A Moscow VETERINARIYA in Russian  
No 4, Apr 91 pp 31-32

[Article by O. F. Rachkova, L. M. Pinchuk and A. L. Lazovskaya, Veterinary Scientific Research Institute of the RSFSR NZ, and V. S. Tyrina, All-Union GNKI; UDC 619:579.873.21.085.2:547.295]

[Text] Identification of mycobacteria down to the species level in cultures grown from pathological material is based on biochemical culture analysis and biological tests on laboratory animals.

Since the 1970s, methods of identifying microorganisms by lipid and fatty acid composition of their cells have been acquiring increasingly greater significance<sup>2, 5</sup>. One of these methods is gas chromatography, which is distinguished by high dependability, reproducibility and swiftness. It requires a minimum amount of bacterial mass grown over any length of time.

The purpose of this paper was to study the possibility of identifying mycobacteria by means of gas-liquid chromatography.

### Materials and Methods

Forty strains were selected for the experiment from the All-Union GNKI [State Control Scientific Research Institute of Veterinary Preparations]. The strains had been obtained from different collections of the world, or deposited at the institute's museum. Prior to the work the strains were verified by biochemical culturing methods<sup>1</sup> and sent to the Veterinary Scientific Research Institute of the RSFSR NZ [not further identified] labeled only in code.

All of the cultures were grown on Levenshtein-Yensen [transliteration] dense egg medium containing short-chain fatty acids, which in certain cases could change the gas-chromatographic fatty acid composition of mycobacteria. Therefore we reinoculated the obtained strains on Pavlovskiy's potato-glycerin medium. Bacterial mass remaining on Levenshtein-Yensen medium was studied by gas-liquid chromatography over the course of a week, at a rate of eight strains a day (the time of one analysis was 40-50 minutes).

A loop was used to transfer 5.0-10.0 mg of the microbial mass to a glass vial, to which several drops (0.1-0.2 ml) of 7 percent tetramethylammonium hydroxide solution in methyl alcohol was transferred. The vial was then sealed shut and heated for 20-30 minutes at 110-120°C. The tetramethylammonium hydroxide caused hydrolysis of lipids and methylation of fatty acids. Then 2.0-5.0 microliters of the material to be analyzed were placed in an evaporator.

Chromatographic analysis was carried out with a Tsvet-152 gas-liquid chromatograph with a flame-ionization detector. The thermostat temperature of the columns in programming mode was from 180 to 280°C, the heating

rate was 8°C per minute, the evaporator temperature was 370°C, and the flow rates were 2.4 liters/hr for the carrier gas and hydrogen and 25 liters/hr for air.

### Research Results

Peaks corresponding to methyl ethers of fatty acids containing from 12 to 26 carbon atoms were obtained on chromatograms of 40 strains of mycobacteria. Presence of long-chain acids containing 22, 24 and 26 carbon atoms was used as the differential criterion for mycobacteria. The cultures under investigation were divided into three groups on the basis of their ratio<sup>4,6</sup>. Dominance of hexacosanoic acid (C<sub>26:0</sub>) over tetracosanoic acid (C<sub>24:0</sub>) was typical of the first group, the reverse was typical of the second, and absence of hexacosanoic acid in lipids was typical of the third. The first group contained *M. tuberculosis* and *M. bovis*, the second contained *M. avium* and *M. intracellulare*, and the third was made up of conditionally pathological and saprophytic mycobacteria.

The identification of cultures by gas-liquid chromatography coincided with the results of biochemical-cultural and biochemical analyses carried out in the GNKI.

Use of bacterial mass from Levenshtein-Yensen medium made it possible to differentiate *M. tuberculosis* and *M. bovis* from other species of mycobacteria within a single day. It was found to be impossible to separate them down to species level using Pavlovskiy's medium. In the case of growth of *M. tuberculosis* and *M. bovis* on liquid synthetic medium, their fatty acid composition differed significantly in relation to content of long-chain acids with an odd number of carbon atoms, chiefly pentacosanoic acid (C<sub>25:0</sub>), and they correspondingly exhibited different C<sub>26:0</sub>/C<sub>25:0</sub> ratios. This ratio was less than or equal to 1 for *M. tuberculosis* and 3-20 or more for *M. bovis*<sup>3</sup>.

Differentiation of the strains in the third group requires transfer to Pavlovskiy's medium, since in the case of *M. kansasii* and *M. marinum*, specific double peaks for which the numbers of carbon atoms are C<sub>14</sub> and C<sub>15</sub> are located in the zone of short-chain components. A discrepancy between the results of cultural-biochemical and gas-chromatographic analyses was noted for two strains. The specificity of the method was 95 percent.

### Conclusion

Gas-chromatographic analysis of the fatty acids of mycobacteria makes it possible to identify them down to species level, or to separate them into pathogenic, conditionally pathogenic and saprophytic groups of microorganisms in genus *Mycobacterium*. This method may be used to screen mycobacterial infections over large territories.

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### Composition and Metabolic Activity of Association of Bacteria That Decompose Diethylene Glycol

927C0239A Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 53 No 3, May-Jun 91 (manuscript received 11 Jun 90) pp 30-38

[Article by S. A. Sedina and V. N. Ivanov, Institute of Microbiology and Virology, Ukrainian SSR Academy of Sciences, Kiev; UDC 574.2]

[Abstract] The objective of this investigation was to select a microbial association that metabolizes diethylene glycol and isolate, identify, and investigate the metabolic activity of its components. Analysis of the associations (sowing once a week for two months on a solid agarose medium with the addition of diethylene glycol) showed that morphological forms of their components did not change much during the entire cultivation period. The associations were cultivated in a chemostat using three regimens to find those most resistant to diethylene glycol. Analysis of morphological, cultural, physiological, biochemical, and other characteristics revealed that the strains were *Alcaligenes*, *Mycobacterium*, *Rhodococcus*, and *Achromobacter*. The OC-2 strain, determined to be *Mycobacterium*, has straight bacilli 0.5-0.7x2.9-4.0  $\mu$ m and is gram-positive and immobile. It can grow in the presence of 2.5 percent NaCl. The optimal growth temperature is 30°C, and the optimal pH is 7.0-7.2. It can utilize diethylene glycol as a growth substrate. Strain AC-1, *Rhodococcus*, has bent bacilli 0.9-1.0x4.8-5.2  $\mu$ m in size and is gram-positive and immobile. It can grow in the presence of 2.5 percent NaCl. The optimal growth temperature is 25-30°C, and the optimal pH is 7.0-7.2. It can utilize diethylene glycol as a growth substrate. Strain LV-1, *Alcaligenes paradoxus*, has gram-negative, mobile bacilli 2.7x0.9  $\mu$ m in size and can grow in 2.5 percent NaCl. It grows best at 25-30°C and pH of 7.0-7.2. Strain TS-1, *Achromobacter iophagus*, has gram-negative mobile bacilli 0.6-1.0x1.6-2.5  $\mu$ m in size and grows best at 20-30°C and pH

7.0. Investigation of the possible pathways for the transformation of diethylene glycol by an association of microorganisms revealed two pathways for diethylene glycol metabolism. The results demonstrated that bacteria that decompose diethylene glycol, OC-2, AC-1, and LV-1, assimilate ethylene glycol well as a sole source of carbon. The findings suggest that decomposition of diethylene glycol by a selected bacterial association occurs through the formation of ethylene glycol. In addition, it was shown that *A. paradoxus* LV-1 plays the primary role in the decomposition of diethylene glycol, working ten times faster than OC-2 and AC-1. Figures 2; tables 4; references 24: 10 Russian, 14 Western.

### Destruction of Cable Paper by Cellulose-Decomposing Bacteria

927C0239B Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 53 No 3, May-Jun 91 (manuscript received 29 May 90) pp 87-91

[Article by L. P. Purish, I. A. Kozlova, O. A. Lunev, and Ye. I. Andreyuk, Institute of Microbiology and Virology, Ukrainian SSR Academy of Sciences, Kiev; Kiev Branch, Communications Scientific Research Institute; UDC 579.69.620.193.8]

[Abstract] The effect of cellulose-decomposing bacteria and their association with sulfate-reducing bacteria on Finnish experimental and serial and Soviet cable papers used as isolating covers in plated cables with a lead sheath was investigated using an association of cultures of these bacteria isolated from the second layer of a corroded plate of a cable line. The authors then obtained a binary culture of cellulose-decomposing bacteria consisting of bacilliform and clostridial forms. It was found that copper naphthenate in different species of cable paper affected the bacteria differently. The results demonstrated that cellulose-decomposing bacteria reproduced three to four times more actively in a cellulose-free medium where the sole source of carbon was cable paper in the medium, thus suggesting that the cable paper used as a protective cable covering may be a nutritive substrate for cellulose-decomposing bacteria. These findings also showed that sulfate-reducing bacteria grew very actively despite the fact that organic substances necessary for the vital activity of this group of bacteria were not added to the medium. In addition, cellulose-decomposing bacteria form organic acids during their vital activity that can be used by sulfate-reducing bacteria as sources of carbon. In summary, the results demonstrated that paper strength decreases as the amount of bacteria increases. Therefore, these types of cable paper are not bioresistant with respect to cellulose-decomposing bacteria and cellulose-decomposing bacteria-sulfate-reducing bacteria associations and clearly do not adequately protect the cable from bacterial damage. Figures 3; tables 2; references 5: 3 Russian, 2 Western.

**Effect of Corrosive Bacteria on Physico-Mechanical Properties of Coal Composites**

927C0239C Kiev *MIKROBIOLOGICHESKIY ZHURNAL* in Russian Vol 53 No 3, May-Jun 91 (manuscript received 19 Jul 90) pp 91-95

[Article by Zh. P. Kopteva, V. V. Zanina, A. Ye. Kopteva, A. G. Tsaur, and Ye. I. Andreyuk, Institute of Microbiology and Virology, Ukrainian SSR Academy of Sciences, Kiev; Eastern Coal Chemistry Institute, Sverdlovsk; UDC 579.69:620.193.8]

[Abstract] The effect of associations of corrosive bacteria on the physico-mechanical properties of polymeric coal composites was investigated using three composites with coal pitch, oil, and fillers. Composite No. 1 also had vat residues of styrene rectification (VRSR); No. 2 had a polyurethane polymer; and No. 3 had rubber powder. The effect of the denitrifying, sulfate-reducing, and carbohydrate-oxidizing bacteria on protective properties was investigated in liquid media. It was shown that all

test cultures actively developed in elective media in the presence of the coal composites in question. With composite No. 1 the numbers of all bacteria increased by one to two orders of magnitude. The sulfate-reducing bacteria accumulated 204 mg/l hydrogen sulfide. The number of bacteria increased by two orders of magnitude with composite No. 2. Composite No. 3 with the rubber powder increased bacteria numbers by four orders of magnitude. The sulfate-reducing bacteria accumulated 212.5 mg of hydrogen sulfide per milliliter of medium. The results demonstrated that the physicochemical properties changed only slightly in spite of the intensive growth of test cultures in the media with composites. In conclusion, the findings showed that the coal composites have no bactericidal effect with respect to corrosive bacteria. The results suggest that composites with a polyurethane polymer and polymers of VRSR can be used as an effective means of protecting metal and metal structures from microbial corrosion. Figures 1; tables 1; references 12: 9 Russian, 3 Western.



**DNA Hybridization With Oligonucleotides Immobilized in Gel: Convenient Method for Recording Single Base Pair Substitutions**

927C0230A Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 25 No 3, May-Jun 91 (manuscript received 20 Mar 91) pp 718-730

[Article by K. R. Khrapko, A. A. Khorlin, I. B. Ivanov, B. K. Chernov, Yu. P. Lysov, S. K. Vasilenko\*, V. L. Florentyev, and A. D. Mirzabekov, Molecular Biology Institute imeni V. A. Engelgardt, USSR Academy of Sciences, Moscow; \*All-Union Scientific Research Institute of Molecular Biology, USSR Ministry of the Medical Industry, Novosibirsk Oblast, Koltsovo; UDC 577.323]

[Abstract] This study is part of a program in the development of sequencing hybridization with an oligonucleotide matrix. The paper presents methods for the immobilization and hybridization of oligonucleotides. In order to develop a method for analyzing DNA sequences by means of hybridization with a large number of oligonucleotide probes, short (8 base) oligonucleotides were immobilized in a 30  $\mu$ g thick layer of 8 percent polyacrylamide gel fixed to a glass plate. The results demonstrated that hybridization of radioactively and fluorescently labeled DNA fragments with immobilized oligonucleotides makes it possible to differentiate single DNA base substitutions in an effective manner. It was also revealed that the rinsing temperatures of the duplexes depend on the concentrations of the immobilized oligonucleotide, which makes it possible to balance the rinsing temperatures for duplexes varying in their GC composition with a set of concentrations. In order to make the system more compact "hybridization chips" or disks were made on which the gel was arranged in the form of a quadratic matrix with a density of nine points per 1 mm<sup>2</sup>. This miniaturization of the oligonucleotide matrix conserves oligonucleotide material and automates the procedure of hybridization, rinsing, and reading and analysis of information. Using the "chips" made it possible to attain a sensitivity of 20 attomoles per point with a fluorescently labeled probe. The use of these oligonucleotide matrices makes this practical procedure simple and convenient. In addition, the fluorescent label simplifies the process of reading information. Perspectives for the development and application of this approach are discussed. Figures 6; tables 1; references 17: 3 Russian, 14 Western.

**Identification of Protein Product From Novel Human *Son* Gene and Biological Effect When Altered Form of This Gene Is Injected Into Mammalian Cells**

927C0230B Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 25 No 3, May-Jun 91 (manuscript received 28 Nov 90) pp 731-739

[Article by I. M. Chumakov, F. B. Berdichevskiy, N. V. Sokolova, M. V. Reznikov, and V. S. Prasolov, Molecular Biology Institute imeni V. A. Engelgardt, USSR Academy of Sciences; UDC 577.21.29]

[Abstract] Novel approaches to researching the functional role of the *son* gene and identifying its protein content involved fibroblasts from Balb/c, NIH3T3, and  $\psi$ -2 mice and *Rat2* rats and human kidney cells transformed with adenovirus type 5, line 293. The cells were cultivated in a DMEM medium containing 10 percent embryonal bovine serum in 5 percent CO<sub>2</sub> at 37°C. The results demonstrated that the *son* gene protein product is present in human and animal cells, which opens the door to researching the role of this gene in cell metabolism and its interaction with other proteins, and explaining the functional significance of its homology with the *mos* and *myc* genes. In order to develop the concept of the possible role of the *son* gene in mammalian cells, a construction was produced based on the retrovirus vector pPS-*neo*, thus making it possible to express the 3'-terminal end of the *son* gene transcript. The data also showed that the biological activity of a shortened *son* gene fragment is expressed in the change in morphology and the nature of fibroblast growth in the tissue culture. Experiments involving the implantation of cells from lines NIH3T3, NCC2, B2, and A1 in thymectomized mice revealed that along with morphological changes in cells given the *son* gene, the pPS-*son* retrovirus vector has an altered tumorigenic status in comparison with the acutely malignant NCC2 cells. In addition, it was shown that NCC2 cells were the most tumorigenic, NIH3T3 cells were moderately tumorigenic, A1 cells were slightly tumorigenic, and B2 cells were non-tumorigenic. A novel protein with a molecular mass of 120 kD and protein p92<sup>son</sup>, which reacts with *son*-specific antiserum, were found in the transfectant cells. In conclusion, the complex pattern of expression may point toward the regulatory role of this gene in cellular proliferation and differentiation processes in higher eukaryotes and its involvement in controlling the malignant regeneration of cells. Figures 5; tables 1; references 9: 3 Russian, 6 Western.

**Complexity Analysis of Genomes. 1. Complexity Measures and Classification of Detected Structural Regularities**

927C0230C Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 25 No 3, May-Jun 91 (manuscript received 11 Jan 91) pp 825-834

[Article by V. D. Gusev, V. A. Kulichkov, and O. M. Chupakhina, Mathematics Institute, Siberian Department, USSR Academy of Sciences, Novosibirsk; All-Union Molecular Biology Scientific Research Institute, "Vektor" Scientific Production Association, USSR Ministry of the Biomedical Industry, Koltsovo, Novosibirsk Oblast; UDC 577.212.2]

[Abstract] The objective of this investigation was to describe a method of identifying structural regularities using measures C<sub>1</sub> and C<sub>2</sub> and classifying these regularities and to discuss the functional significance of the detected fragments. This study investigates only abnormal fragments with minimal complexity. The authors analyzed approximately 30 complete genomes of the simplest prokaryotic and eukaryotic microorganisms. The most typical regularities are: 1. a series of repeating homogenous

fragments (periodicity); 2. abnormally low frequency of use of individual elements of alphabet; 3. predominance of a given *l*-gram over the rest; 4. spaced repetitions; 5. palindrome-hairpin structures, symmetries, and block symmetries; and 6. repetitions of complementary palindromes and symmetries. The variety of types of detected regularities confirms the hypothesis about accumulated properties of complexity measures. Complexity analysis may be viewed as a universal tool for identifying local and integral structural regularities in the primary structures of nucleic acid molecules. However, the functional significance of the abnormal fragments is not always obvious. Finally, most complex fragments gravitate toward gene centers. Figures 8; references 6: 5 Russian, 1 Western.

### Spatial Structure of Apamin in Solution

927C0294A Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 4, Jul-Aug 91  
(manuscript received 30 Nov 91) pp 937-945

[Article by A. M. Andrianov and A. A. Akhrem, Institute of Bioorganic Chemistry, Belorussian SSR Academy of Sciences, Minsk; UDC 577.322.5]

[Abstract] NMR spectroscopic data was employed in combination with the tenets of molecular mechanics to assess the low-energy conformational features of apamin, a neurotoxic peptide derived from the honeybee *Apis mellifera*. Key conformational features of the peptide backbone were found to be determined by the combination of a type III  $\beta$ -bend formed by amino acid moieties 5-8, and a right-handed  $\alpha$ -helix formed by moieties 9-18. These two segments are separated by an intermediate reverse flexure formed by residues 5-8. A model of the molecular conformation was derived based on possible hydrogen bonds and 2-D spectroscopy of the Overhauser effect. Figures 3; tables 3; references 48: 15 Russian, 33 Western.

### Vaccinia Virus Proteins Associated With Plasma Membranes of Infected Cells

927C0294B Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 4, Jul-Aug 91  
(manuscript received 06 Dec 90) pp 946-954

[Article by N. V. Cheshenko, N. A. Netesova and E. G. Malygin, "Vektor" Scientific Industrial Association, All-Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast; UDC 576.8.098:577.1]

[Abstract] Conventional techniques of affinity chromatography and gel electrophoresis were employed in studies on vaccinia WR proteins isolated from plasma membrane of infected BHK-21 cells. Immunochemical analysis demonstrated the proteins p35, p34 and p23 represented early-late proteins, while proteins p45, p42, p40, p60 and p28 were late proteins. Immunochemical analysis of products obtained in a cell-free translation system showed that 33 and 30 KD proteins are possible precursors of p60 and p34, while p40 and p45 may share a common precursor protein (27 KD) with p35. However, at this time antisera against p42, p28 and p23 did not react with any translation products, indicating that other methods may have to be employed to identify their precursor proteins. Figures 6; tables 2; references 19: 6 Russian, 13 Western.

### Structural Studies on Recombinant Human INF-A Using Fluorescence Polarization, Circular Dichroism and Differential Microcalorimetry

927C0294C Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 4, Jul-Aug 91  
(manuscript received 04 Feb 91) pp 1061-1070

[Article by I. V. Dudich, Ye. I. Dudich, D. P. Kulevatskiy and V. P. Zavyadov, Institute of Immunology, USSR Ministry of Medical Industry, Lyubuchany, Moscow Oblast; UDC 577.322.24]

[Abstract] Structural studies were conducted on recombinant human rIFN- $\alpha$  employing fluorescence polarization, circular dichroism and differential microcalorimetry. The resultant data demonstrated that at neutral pH values rIFN- $\alpha$  exists in the form of a dimer, and at pH < 5 as a monomer. Further, rIFN- $\alpha$  is capable of complete renaturation as pH is adjusted from 3.0 to pH 7.5. Calorimetric studies showed that the enthalpy of heat denaturation was 306 kJ/mole and reflected a two-stage process. Accordingly, the tertiary structure of rIFN- $\alpha$  has been shown to consist of two thermodynamic domains which melt independently and cooperatively. On balance, the resultant data indicate that rIFN- $\alpha$  is a rigid ellipsoid with a 4:1 axial ratio, consisting of two cooperative domains of limited mobility. Figures 6; tables 3; references 20: 4 Russian, 16 Western.

**Impact of Decimeter Waves on Nuclear DNA  
From Cerebral Cortex Cells**

927C0197A Moscow VOPROSY KURORTOLOGII,  
FIZIOTERAPII I LECHEBNOY FIZICHESKOY  
KULTURY in Russian No 4, Jul-Aug 91 (manuscript  
received 11 Apr 91) pp 20-23

[Article by O. A. Krylov, S. V. Rutsay, L. V. Mikhaylik,  
and N. V. Tverskova, All-Union Research Center for  
Medical Rehabilitation and Physical Therapy, Moscow;  
UDC 615.849.11.015.4:612.825.014.22].076.9]

[Abstract] The objective of this investigation was to determine which sections of nuclear DNA from cerebral cortex cells are most responsive to the impact of an electromagnetic field with a decimeter wave range. Forty mongrel male rats (180-200 g) raised under identical conditions were selected from a single shipment and then separated into experimental and control groups. Animals in the experimental group were fastened to a special stand. A 40 mm radiating element was oriented along the axial line of the body and firmly affixed to the head. The head was irradiated with a Romashka electromagnetic signal generator, 460 MHz, flux density power of 1 W/cm<sup>2</sup> and specific absorbed power of 84 +/- 5 W/kg for 10 min. <sup>3</sup>H-Thymidine labeled DNA precursors were injected intraperitoneally in 0.3 ml physiological solution in a dose of 0.25 mCi three hours prior to radiation exposure. The radioactivity of labeled DNA was measured using a scintillation counter in a mixture with a known amount of DNA, and chromatography was used to separate the denatured and renatured DNA. The results showed that decimetric wave radiation increases the renaturation rate for unique DNA sequences. There was a 16 percent increase in <sup>3</sup>H-thymidine incorporation in the DNA of cerebral cortex cells, which suggests intensification of DNA synthesis in these cells. Thus, the findings demonstrated that decimetric wave radiation increases the number of unique and moderately repetitive DNA fragment sequences and respectively the intensification of DNA synthesis. Figures 2; tables 1; references 17: 12 Russian, 5 Western.

**Experimental Investigation of Effect of  
Low-Intensity, Millimeter Range UHF  
Electromagnetic Radiation on Metastasis Process  
in Malignant Tumors**

927C0197B Moscow VOPROSY KURORTOLOGII,  
FIZIOTERAPII I LECHEBNOY FIZICHESKOY  
KULTURY in Russian No 4, Jul-Aug 91 (manuscript  
received 15 Apr 91) pp 23-27

[Article by A. Yu. Smirnov, S. V. Zinovyev, and V. M. Bogolyubov, All-Union Oncology Research Center, USSR Academy of Medical Sciences; All-Union Medical Rehabilitation and Physical Therapy Research Center, USSR Ministry of Health, Moscow; UDC 615.849.11.036:616-066.04-033.1].076.9]

[Abstract] The possible impact of low-intensity, millimeter range UHF electromagnetic radiation on the metastasis process and life span was investigated in female A/SNL mice aged two to three months (20-22 g) which had been injected with a very metastatic tumor, substrain VMR-mg, in the femoral muscle. The mice were irradiated through a horn antenna with the horn placed two to three mm from the animal for one hour. The flux density of the delivery power was 12.5 mW/cm<sup>2</sup>. The electromagnetic field was generated at a 7.09-7.12 mm wavelength, 50 Hz. The experiments were performed daily for five days, beginning five days after the tumor cells were injected. An investigation of the intensity of VMR-mg strain metastasis in 15 different areas revealed a 25-60 percent decrease in metastasis activity in all areas investigated. The authors conclude that it is difficult to understand the effect of low-intensity millimeter range UHF electromagnetic radiation on the metastasis process. Several possible factors which were not taken into account and which may affect the results were discussed. Figures 4; tables 1; references 9: 8 Russian, 1 Western.

**Biomedical Aspects of Using Posthumous Blood**

927C0191A Minsk VESTNIK AKADEMII  
MEDITSINSKIKH NAUK SSSR in Russian  
No 9, Sep 91 (manuscript received 01 Nov 90) pp 18-24

[Article by V. B. Khvatov, Emergency Care Scientific Research Institute imeni N. V. Sklifosovskiy, Moscow; UDC 615.388.03]

[Abstract] This report presents a biomedical description of blood and blood plasma obtained from people who have died suddenly. Early research in this field proved that blood from people who had suddenly died remained sterile and non-toxic for 24 hours. Investigation of biochemical parameters indicated that this blood is suitable for clinical use. It has been shown that posthumous blood has more sugars, residual nitrogen, cholesterol, free hemoglobin, and potassium ions, and that it has a higher concentration of lipids and inorganic phosphorus. In addition, posthumous blood has been demonstrated to exert a therapeutic effect on various types of hemorrhages. It is a good anti-shock agent for use before, during, and after operations. The three primary directions for the development of the use of posthumous blood include: 1. biochemical, biophysical, and immunochemical research on posthumous blood. Clinical and section data are governing factors in the objective assessment of some pathological processes in thanatogenesis. 2. Production, description, and clinical use of posthumous blood components. 3. Fibrinolytically active plasma preservation. Posthumous blood plasma and perfusate are the specific raw materials for producing the fibrinolytic agent and the products of fibrinogen-fibrin degradation. The fibrinolytic potential of posthumous blood plasma is due to the plasminogen activator. It is a glycoprotein with the electrophoretic mobility of beta-globulins with a mass of 65-75 kD and an isoelectric point at pH 6.2. It was shown that the intravenous administration of plasma kinase to animals results in an increase in fibrinolytic activity and a decrease in the coagulation and anti-protein kinase potential of the blood. Other research showed that albumin and gamma globulin from posthumous blood meets the standards set for donor blood but has a 55-65 percent lower polymer content. As a whole, the cost of products obtained from posthumous blood is 2.7 times less than for donor blood. In conclusion, the data demonstrate the feasibility, sense, and promise of using components, preparations, and biologically active substances from the blood plasma of persons who have suddenly died. Figures 1; tables 1; references 53: 42 Russian, 11 Western.

**Pattern of Changes in Systemic Hemodynamic Parameters in Response to Combined Action of Vasoactive Substances**

927C0233A Kiev FIZIOLOGICHESKIY ZHURNAL  
in Russian Vol 77 No 4, Apr 91 (manuscript received 19 Oct 89) pp 24-33

[Article by M. V. Lioznov and B. I. Tkachenko, Chair of Normal Physiology, First Leningrad Medical Institute imeni Academician I. P. Pavlov, Leningrad; UDC 612.13+577.15/1.17]

[Abstract] The pattern and magnitude of shifts in the total peripheral resistance of vessels, cardiac output, and total venous return of blood to the heart and blood flows of the anterior and posterior vena cavae in response to the combined action of noradrenaline (1-64  $\mu\text{g/kg}$ ) and angiotensin (0.25-8  $\mu\text{g/kg}$ ) were investigated in two series of acute experiments on cats (3-5 kg). The results demonstrated that the magnitude of changes in the total peripheral resistance of vessels in response to combined simultaneous injection of noradrenaline and angiotensin is greater in unison than individually. However, changes in cardiac output revealed a different aspect of shifts in this parameter in comparison with changes in the total peripheral resistance of vessels and arterial pressure. In addition, the combined intravenous injection of these two pressor substances altered the blood flow in the posterior vena cava to a greater degree than was found with the shifts of this parameter in response to the individual action of these substances. In order to determine whether shifts in the arterial and venous sections of the systemic vascular bed in response to vasoactive substances were specific to the pressor agents alone, a second series of experiments investigated the magnitude of changes of the same parameters in response to the combined depressor agents acetylcholine chloride (0.001-10  $\mu\text{g/kg}$ ) and histamine dichloride (0.5-16  $\mu\text{g/kg}$ ). It was shown that changes in the systemic arterial pressure and total peripheral resistance of vessels in response to the combined depressor agents together were no greater than changes elicited by each substance individually. Consequently, the data demonstrated that this pattern of changes in the parameters of the arterial section of the vascular system in the response of the circulatory system to two vasoactive substances is inherent to the combinations of both pressor and depressor stimuli. But in the venous section of the vascular system, this pattern of changes in the parameters is displayed regardless of the direction or degree of changes in the arterial pressure. This suggests that this pattern of changes in response to vasoactive stimuli is governed by the direct effect of humoral stimulation on the vascular myocytes. In conclusion, these results indicate a different pattern of changes in the arterial and venous sections of the vascular system in response to combinations of two vasoactive humoral stimulants that cause unidirectional changes in systemic arterial pressure. Figures 4; tables 2; references 21: 12 Russian, 9 Western.

**Ethologopharmacological Description of Central M-Cholinolytics**

927C0233B Kiev FIZIOLOGICHESKIY ZHURNAL  
in Russian Vol 77 No 4, Apr 91 (manuscript received 04 Jun 90) pp 109-112

[Article by S. I. Kremenevskaya, E. P. Zatsepin, and S. M. Korolev, Laboratory of Applied Pharmacology, Toxicology Institute, USSR Ministry of Public Health, Leningrad; UDC 612.014.421:612.118.2]

[Abstract] The effects of central M-cholinolytics on orientating and conditioned reflex activity in female mongrel rats were compared under conditions of a 100 cm diameter open field using integral evaluation of animal behavior. The compounds were injected intramuscularly in doses ranging from ineffective to ED<sub>99</sub>. It was found that dextrorotatory benzetimide was more active than levorotatory benzetimide. The results demonstrated that all M-cholinolytics investigated impaired the orientating reflex in rats by several-fold and in a number of cases they surpass those that upset the negative conditioned reflex. Data obtained from investigating the effect of the benzetimide isomers on rat behavior suggest that the method of assessing the negative conditioned reflex for M-choline blockers is more sensitive than the method of assessing the orientating reflex. In conclusion, the correlation dependence between the activity of M-cholinolytics that impair animal behavior and their central M-cholinolytic activity indicate that blockage of M-choline receptors underlies disturbances in M-cholinolytic behavior. Tables 2; references 5: 4 Russian, 1 Western.

#### Catecholamine and Serotonin Neurotransmitters in Plants

927C0233C Moscow *USPEKHI SOVREMENNOY BIOLOGII* in Russian Vol 111 No 4, Apr 91 pp 622-636

[Article by V. V. Roshchina, Cellular Biophysics Institute, USSR Academy of Sciences, Pushchino, Moscow Oblast; UDC 581.1:577.175.82]

[Abstract] The objective of this article was to summarize the experimental data gathered to date on the function of catecholamines and serotonin in plants. Catecholamines have been found in 27 species of plants in 16 families, while serotonin has been found in 33 species in 14 families. The bulk of catecholamines and serotonin in nerve cells is concentrated in secretory vesicles covered with klatrin [as published] protein. These vesicles have also been found in plants. The pathways by which catecholamines and serotonin are formed from phenylalanine and tryptophane, respectively, are discussed. Research has shown that metabolic processes may be driven by the deactivation of biogenic amines as well as by the formation of toxic products, alkaloids. Investigation of the effects of catecholamines and serotonin on plants showed that dopamine can suppress or completely block the growth of callous tissue, depending on dose. Serotonin has been shown to be an active growth regulator, while catecholamines regulate the processes of development and morphogenesis. Other research has found that adrenaline, noradrenaline, and serotonin alter the membrane potential of *Nitella syncarpa* green algae cells. In addition, biogenic amines may affect the metabolism of plant cells by regulating enzyme activity or by being incorporated as a precursor in the reaction. Also, catecholamines and serotonin display a protective role under life-threatening conditions. In conclusion, the

presence in plants of catecholamine and serotonin neurotransmitters, their physiological activity, and the discovery in plant cells of individual dopaminergic, adrenergic, and serotonergic regulatory system components known to exist in animals suggest the general biological role of these substances in irritability. Basic directions for future studies are outlined. Figures 3; tables 3; references 120: 23 Russian, 97 Western.

#### Prevention and Non-Opiate Leu-Enkephalin Analog Correction of Prenatal Hypoxia-Induced Impairments in Livers of Albino Rat Progeny

927C0292C Moscow *BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY* in Russian Vol 112 No 9, Sep 91 (manuscript received 13 Mar 91) pp 296-298

[Article by L. I. Utkina and S. S. Timoshin, Central Scientific Research Laboratory, Khabarovsk Medical Institute; UDC 618.33-008.92271-008.64-07:[616.36-091+616.36-092]-053.31]

[Abstract] The involvement of free radical processes in altering proliferation in the liver of newborn progeny of albino rats subjected to chronic hypoxia as well as the possibility of prenatal correction of these impairments using a neonatal leu-enkephalin analog were investigated. Preliminary research demonstrated that prenatal chronic hypoxia causes a decrease in newborn rat body weight and an increase in liver mass. The liver lagged behind in gestation periods, as a result of which the hemopoietic role increases under conditions of hypoxia, as indicated by a two-fold increase in the area of hemopoietic tissue while the area of the parenchyma decreased by 10 percent due to suppression of proliferative processes. Intrauterine chronic hypoxia also caused intensification of lipid peroxidation, as evidenced by a 2.7-fold increase in the malonic dialdehyde concentration in the newborn rat liver. The results showed that administering the leu-enkephalin analog Phe-Dala-Glu-Phe-Le-Arg in a dose of  $2.7 \times 10^{-9}$  M prevented the development of prenatal hypoxia and an increase in liver mass. It also prevented the development of functional immaturity. However, administering the hexapeptide did not bring about complete normalization: the area of hemopoietic tissue was 1.3 times larger than the control. In addition, investigation of lipid peroxidation in the liver indicated that a certain part of the protective effect of the hexapeptide may be attributed to attenuation of peroxidation activity and an increase in antioxidant activity. It was also shown that administering the hexapeptide to pregnant female rats not subjected to hypoxia did not induce any proliferative alterations in the hepatocytes. In conclusion, this hexapeptide was assessed to exhibit a cytoprotective effect. Tables 2; references 14: 13 Russian, 1 Western.

### Monosynaptic Connections: Opioid Effects on Plasticity of Presynaptic Neurons and Defined Synapses

927C0293A Moscow ZHURNAL VYSSHEY NERVNOY DEYATELNOSTI IMENI I.P. PAVLOV in Russian Vol 41 No 4, Jul-Aug 91 (manuscript received 12 Aug 90; in final form 31 Oct 90) pp 788-795

[Article by T. L. Dyakonova and G. G. Arakelov, Institute of Developmental Biology, USSR Academy of Sciences; Chair of Psychophysiology, Moscow State University; UDC 612.822.3+612.8.015]

[Abstract] The edible snail *Helix lucorum* was employed in studies on the effects of opioids on neuronal plasticity. The electrophysiologic measurements were performed on the monosynaptic connections involving the neuron pairs LPa7-LPa3, LPa7-PPa3, LPa8-LPa3 and LPa8-PPa3. The results showed that every components of the system—presynaptic neurons, synapses, postsynaptic neurons—responded with habituation to rhythmic electric stimuli delivered by intracellular electrodes. Introduction of  $10E-6$  to  $10E-4$  M leu- or met-enkephalin acted in an identical manner on LPa7 and LPa8, slowing onset of habituation to control levels. The amplitude of postsynaptic potentials of neurons LPa3 and PPa3 also diminished. However, a direct connection between these two events was not apparent since at times habituation of presynaptic neurons was not affected by the enkephalins while that of postsynaptic neurons was, and vice versa. In addition, reduction in the duration of evoked postsynaptic potentials provided further evidence that the enkephalins altered synaptic plasticity. In all respects, the two enkephalins behaved in

an identical manner in altering neuronal plasticity. Figures 5; references 16: 12 Russian, 4 Western.

### Modulation of Short-Term Plasticity of Neuronal Cholinoreceptors by Arachidonic Acid and Acyclic Arachidonic Metabolites in Edible Snails

927C0293B Moscow ZHURNAL VYSSHEY NERVNOY DEYATELNOSTI IMENI I.P. PAVLOV in Russian Vol 41 No 4, Jul-Aug 91 (manuscript received 03 Dec 90; in final form 09 Jan 91) pp 796-805

[Article by A. S. Pivovarov, Ye. I. Drozdova and B. I. Kotlyar (Dec), Chair of Higher Nervous Activity, Biological Faculty, Moscow State University; UDC 612.822.1+615.78+62.822.3]

[Abstract] An analysis was conducted on short-term modulation of plasticity of cholinergic neurons PPa3 and LPa3 of the snail *Helix lucorum* by arachidonic acid and arachidonic metabolites. Modulation by metabolites was assessed in terms of the effects of treatment of the cells with phospholipase A (quinacrine), lipoxygenase (nordihydroguaiaretic acid) and cyclooxygenase (indomethacine) inhibitors. The double clamp studies demonstrated that arachidonic acid and the inhibitors diminished acetylcholine-induced inward currents. However, while arachidonic acid potentiated extinction of inward currents, the results with the inhibitors—which determined the metabolic fate of arachidonic acid—indicated that cyclic metabolites (prostaglandins, thromboxanes, prostacyclins) do not modulated cholinoreceptor plasticity, whereas acyclic do. Figures 5; references 21: 2 Russian, 19 Western.



### Use of New Economic Program in Grodno Oblast Clinical Hospital

927C0191C Minsk ZDRAVOOKHRANENIYE  
BELORUSSII in Russian No 8, Aug 91 (manuscript  
received 29 Apr 91) pp 28-29

[Article by V. A. Rozhko, Grodno Oblast Clinical Hospital; UDC 614.2:362.11(476.6)]

[Abstract] The objective of the new economic program instituted in the Grodno Oblast Clinical Hospital was to alter the financing and planning of the hospital and to introduce a rigid system of quality control for medical care and to scale pay based on the end results. The program began January 1, 1990, and involved the training of physicians, nurses, and personnel. The program went quite well after problems with the budget and negotiating for services were resolved. During this time there were no substantiated complaints against the personnel. The surplus funds earned were used for employee bonuses and benefits. In conclusion, the results show that the new economic program facilitates improved quality in the treatment and diagnosis process and enhanced medical service. It demands that medical personnel act in a professional manner and take a new approach to organizing the public health care structure. Tables 1.

### Russian Law Requires Licensing of Physicians

927C0248A Moscow ROSSIYSKAYA GAZETA  
in Russian 21 Dec 91 p 3

[Article by Yana Yurova under the rubric "Be Healthy":  
"Patients, Do Not Demand the 'Complaints Book'"]

[Excerpts] The Law Concerning Medical Insurance for Russian Citizens will be in effect by 1993. Of course, it has long been apparent to everyone that there is a need for reform of our inefficient health care. However, it would be naive to believe that a new progressive law will immediately solve all problems.

One of the most long-standing flaws of our medicine is the inadequate qualifications of most specialists. Upon issuing a certificate concerning education, the VUZ [institution of higher learning] sheds all responsibility for the work performance of its former student. [passage omitted]

The medical insurance law provides for licensing of medical institutions. This will be done by a social-professional organization, the insurance company and a state institution. There are also provisions for evaluating the performance of medical personnel and adequacy of supply of equipment at the institutions. Thus, a rating will be established for each clinic and hospital, and a unique "table of ranks" will be compiled. Accordingly the ratings will vary in them.

What is the guideline that is to be used for licensing physicians? It includes two stages: determination of education level of each specialist and anonymous testing. The

selection of questions should conform to world standards established for physicians in different specialties.

And this is where a problem arises. It is no secret to anyone that, at the present time, the level of qualifications of our practicing physicians is rather low in most cases. After strict and exacting screening, their ranks will diminish appreciably. However, this not only will fail to solve all problems, but will add some: after all, there is already a shortage of physicians in Russia. Especially since, in addition to the usual quacks, some good specialists could be sifted out because, for some reason or other, they did not learn new techniques, or simply because they were not taught, for example, to keep informed about new ideas. In order to help physicians, they should be trained in advance for certification and licensing.

This is expressly the suggestion offered by the Association of Pediatric Neurologists, a social-professional organization founded a year ago at the Moscow Pediatric Neurological Consultation Polyclinic. It suggested that in 1992 the Russian Ministry of Health train and certify pediatric neurologists in Moscow alone for the time being, by means of testing programs. And starting in 1993, it should also begin to license specialists. This idea was supported by the Main Health Care Administration, as well as the permanent commission of the Moscow Council.

The Association of Pediatric Neurologists has elaborated and proposed a program for specialist training for certification and licensing in the simplest form, without taking time off work. It consists of short educational cycles repeated several times a year. After each cycle, there would be tests and certificates would be issued, confirming a specific level of knowledge.

The association will assume the task of organizing these cycles, in collaboration with the Organizational and Methodological Center for Pediatric Neurology of Moscow. It is planned to call upon the pedagogic staff of the Department of Pediatric Neurology of the Russian University imeni N. I. Pirogov and Central Institute for Advanced Training of Physicians to teach these classes. It is expected that this training will be free to neurologists. True, we still do not know who will finance the program.

The Association of Pediatric Neurologists considers all this work to be merely the minimal goal for the time being. We were told by the deputy chairman of the association, Yevgeniy Kessel, chief of the City Pediatric Neurological Consultation Polyclinic: "Our future plans include organization of a continuous system of assessing education. The procedure for testing all specialists should be repeated at least once every three years. After all, a diploma is also subject to inflation, like the ruble; new techniques, new drugs and new forms of diseases are constantly appearing in medical practice. New ideas are generated in medicine. Physicians simply must be

informed about all these events. Provided, of course, that they are real physicians and real specialists."

Will you, dear readers, and I live to meet such physicians? Maybe our children will have such luck.

### **Institutional Barriers to New Drugs**

927C0248B Moscow IZVESTIYA in Russian  
22 Nov 91 Union ed. p 4

[Article by L. Ivchenko: "Drugs in a Deadlock: Agency Barriers Prevent Introduction of New Medical Methods"]

[Text] We have been conversing for over an hour already, and we are both tired. Yu. Svishchenko, scientific associate on the Pharmacological Committee, is obviously bored with me. There are files with documents, telephone calls waiting for him, yet I am pestering him about problems of new drugs, which he does not consider to be problems at all.

I am wondering why it takes so long, four to five years, for a drug to become available, why there are two imported products per approved domestic drug, and why the independent [unaffiliated] developer is a persona non grata for the committee. Yet in the opinion of the one in charge of antineoplastic and immunomodulating agents, Yu. Svishchenko, the practices established in the Pharmacological Committee are logical and optimal: there are regulations, in accordance with which all new developments must be submitted following a specific form, they must undergo expert evaluation, and in general one cannot rush in such matters, for we are dealing with the health and safety of people! Yes, the specifications of the Pharmacological Committee are rigid and can be met only by scientists, and for this reason it deals primarily with research institutes, rather than individual authors, let the latter find help at the institutes. As for Kaverin, a judgment has been made by the specialized commission for antineoplastic agents, which was based on the critique of G. Gerasimova, doctor of medical sciences: "The paper submitted is an utterly illiterate compilation, it is absurd." Absurd, you understand? The conclusion of a scientist who heads the department of experimental chemotherapy at the All-Union Oncological Research Center [VONTs]. And the VONTs enjoys the greatest authority in the nation on matters of oncology, and if it pronounces such a sentence for the method, what else can we discuss?

But to me nothing is so unambiguous. Perhaps the reader recalls the article "No One Wanted To Help": (IZVESTIYA, No 215, 1990), which dealt with medical "informants," left to their own resources, whose methods could be beneficial but do not reach patients. The editorial board cited examples of the real help offered to oncological patients by the P. Kaverin, a biologist from Donetsk. G. Gerasimova, doctor of medical sciences, who reviewed Kaverin's paper, states: "Curing people does not serve as grounds to register a product and recommend its use for treatment. This has to be experimentally confirmed. The author must prove the high

antineoplastic activity of the proposed drug, and only then would the commission examine the possibility of using it...."

Proof has to be provided using animals, but mice and rabbits are by no means the laboratory duplicates of man. Gerasimova herself admits that it is possible for a product to help humans but not necessarily affect animals. There are no adequate models. However, Kaverin did carry out animal research as required prior to clinical trials.

"Where are measurements, description of the method, tables, controls? After all, there must be some sort of technology involved! There should be statistics for each experiment. The data he submitted cannot be taken into consideration. And his theory cannot be published, even as a debatable one! What have soluble and insoluble cell proteins to do with it? And what is it?"

Galina Konstantinova [Gerasimova] not only failed to offer any proof of the absurdity of his data (other than her own lack of comprehension), but also voiced the assumption that the cure of the patients, a list of whom Kaverin submitted, "is apparently a fantasy of the author, just like the rest of his data." No one checked the case histories of these patients, no one sought them out or was concerned with the diagnoses. She also did not deem it possible to verify at the institute the antineoplastic effect observed by Kaverin.

"This would evolve into an expensive activity. It would mean postponing scheduled work and starting extra-neous, questionable investigations."

The scheduled topics consist of data for dissertations. And no one wants to give up this main task of all scientific research institutes.

Wherever one looks, one finds a stumbling block. The Pharmacological Committee, to which the roads of new drugs lead, gives the right to evaluate them to expert commissions, which rapidly push away any deviation from what is conventional, and this is understandable: every expert (and one working on a commission as a volunteer at that) represents a scientific institution that does not want to have competitors or have its reputation questioned. The Pharmacological Committee organizes expressly such a system of expertise, where responsibility is not placed on anyone: Scientists have offered their evaluation; what more do you want?

But why do the lone researchers encounter the total indifference of the entire "army" of the Pharmacological Committee headed by its chairman, V. Lepakhin, and why are they only tiresome and boring to him? Are not the members of this agency citizens of their country who are interested in the appearance of new and effective drugs? The answer is simple: The Pharmacological Committee in its present form is strictly a bureaucratic organization, and the substance of bureaucracy is to

shuffle papers, keep track of incoming and outgoing documents, etc.; no interest in science can arise wherever there are clerks at work, rather than researchers, especially if there is a possibility of a trip abroad at government expense to visit firms that produce drugs. V. Lepakhin spends more time abroad than at home! When can he think about Russian science....

As long as the Pharmacological Committee is an official in a department of the Ministry of Health, everything will remain unchanged. We have been deprived of quite a few original products (analogues of which we sometimes purchase abroad) thanks to the Pharmacological Committee, its dogmatism and stagnation. The formula for Karchauli's fluid, which was used with success for treatment of dermal neoplasms, even aggressive malignancy such as melanoma, was lost with the death of its inventor, Doctor A. Yalovoy did not receive a "good" rating for his "company" method of treating tonsillitis. At the suggestion of VONTs, the Pharmacological Committee also rejected the product of N. Kashkin, which prolonged the life of many oncological patients, there being so much written about it! The judgment was the same: nonsense. True, it was expressed more tactfully in writing to Kashkin: the product held no promise because of inadequate therapeutic activity.

The list of such examples could go on and on. The All-Union Research Center for Expert Evaluation of Drugs, which is the present name for the Pharmacological Committee, continues to augment it. A new shingle, new address, new offices, and some new personnel create an illusion of innovation, but it is only an illusion. With respect to development of new drugs, however, he have already come to such a critical point that any postponement of radical changes would lead to an impasse. Nevertheless, as I write these lines, a thought persists that I am writing in vain: the government will not notice the problem, while the Union Ministry of Health (which has never shined with initiative either) is presently worried about its own fate. In our time of political passions, how important can the health of man, of a nation be? Who cares? Could it be that Kashkin and others like him, who want nothing but the welfare of people and to leave a good memory of themselves will remain as our greatest statesmen?

A reader from Krasnodar, N. Kutepov, who responded to our article, proposes a change in the approach to setting wages for scientific associates as a means of bring about a change: Work with developers, with their non-standard, paradoxical proposals, should be advantageous. "It is very simple: remove budgeted financing from the VONTs and switch to remuneration (also from the state budget) for projects and to pay only for new therapeutic or diagnostic methods. Then every author would become the source of existence for the Oncological Center, he will be sought out, rather than rejected. True, this would put an end to the carefree life of scientists, but such a system should be approved for all research centers and institutes...."

This is a very reasonable idea. It is time now for major changes, and one should consider the performance of the former Pharmacological Committee also from the standpoint of the extent to which it represents national and public interests; to cope with this task, it must become a research center. Without a research element, whatever you call it, the Pharmacological Committee is nothing but excess bureaucratic baggage.

#### **Fate of Ophthalmological Center Uncertain**

927C0250A Moscow *ROSSIYSKAYA GAZETA*  
in Russian 9 Jan 92 p 6

[Article by Dmitriy Slobodyanyuk under the rubric "Reporting the Details": "The Apple of Our eyes' Is Hanging by a Thread"]

[Text] The staff of the internationally known complex, "Eye Microsurgery," is winding down the Christmas vacation. The head of this firm, S. N. Fedorov, traveled to the United Arab Emirates on New Year's Eve to earn hard currency needed by the institute. Yet the fate of the "model medical enterprise" is literally hanging by a thread.

In the words of the deputy general director, A. N. Shevchenko, at the very end of last year, a draft of the Ukaze concerning privatization of MNTK [interbranch scientific-technical complex] strangely disappeared within the system of the president. Incidentally, this is already the 17th privatization document transmitted by the institute's management to various structures of government. It is difficult to determine whether this disappearance is related to the usual bureaucratic negligence, but it would seem that privatization of the complex is again deferred.

In the opinion of A. N. Shevchenko, there may be the most unpredictable consequences to this dawdling. The question of financing of the institute by the Ministry of Health of the Russian Federation is still unresolved, but it is obvious that there are insufficient budgeted funds for the "Eye Microsurgery" to survive.

And this means virtually total cessation of operations on Soviet citizens, since only seamy big shots could afford their actual cost.

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#### **First Graduates of Training Course in Support of Voluntary Sterilization Law**

927C0250.B Moscow *TRUD* in Russian 6 Feb 92 p 4

[Interview with Ye. Vikhlyayeva, deputy director of the institute by T. Krivtsova, under the rubric "Mini-Interview: "There Is No Publicity Yet, but Will It Ever Come?"; first paragraph is TRUD introduction]

[Text] "I do not want to have children, and I will not!"—The right to make such a statement had already been given to some Soviet women a year ago, when the

USSR Ministry of Health lifted the ban on voluntary sterilization. But it is only now that training of relevant specialists has been completed at the Russian Scientific Research Center of Perinatologists, Obstetricians and Gynecologists.

[Krivtsova] Are there any restrictions for women who have decided to eliminate their child-bearing capacity for some reason or other?

[Vikhlyayeva] According to existing legislation, we can perform such operations only on women over 30 years of age who have had children.

[Krivtsova] But what if circumstances, for example, health-related ones, change, can the operation be reversed?

[Vikhlyayeva] It is possible to restore child-bearing capacity in 85 cases out of 100. It depends on the method used.

[Krivtsova] Has there been an increase in patients at your center with introduction of the new surgery?

[Vikhlyayeva] Since we began using it only recently, there has not been much increase. There has not been any publicity about it as yet.

[Krivtsova] There are probably many who wonder whether such an operation is humane. After all, we are dealing with the main purpose of women, to be mothers....

[Vikhlyayeva] It is the right of every woman to decide her fate, and the operation to disrupt child-bearing capacity makes it possible to lower the number of abortions that are not always uneventful. Moreover, in our difficult times, there is no need to conceal the fact that an addition to the family is not always a joy....

[Krivtsova] What does voluntary sterilization cost?

The center did not answer this question.

### Mass-Scale Vitamin D Concentrate Poisoning

927C0250C Moscow *RABOCHAYA TRIBUNA*  
in Russian 7 Feb 92 p 2

[Article by Vladimir Romanov, Vologda: "Think Before Taking Something Ill-Placed"]

[Text] In late December of last year, reports began to come from the village of Klimovskoye near Cherepovets about mass scale cases of poisoning. Unfortunately, it was not possible to determine the cause immediately, and the number of victims continued to grow. On 25 January, the oblast management was compelled to seek the help of the president of Russia. Soon after this, the medical specialists of Vologda, together with their colleagues who had arrived immediately from Moscow were able to determine the final diagnosis: "Vitamin D poisoning." It was learned that more than 90 kilograms of vitamin D concentrate had been delivered to the Klimovskoye Poultry Plant, which resembled vegetable oil

in taste and odor. Since there was virtually no verification of integrity of the concentrate, it was taken into homes in the vicinity and added to food. As of today, there are 65 victims, including 14 children. One of the poisoning victims, a 42-year-old woman, expired at the hospital.

Alas, the effects of such poisoning on health are unpredictable as yet. Involvement of internal organs and particularly the kidneys was observed in many of the victims. There was deposition in the body of large amounts of calcium. Although the prognosis of the physicians is optimistic, in the sense that there would be no more fatalities, they do not rule out the possibility that some of the victims will be disabled.

What lesson do we glean? The specialists are warning the inhabitants of that oblast: do not buy vegetable oil from private sources or at markets, since some amounts of the concentrate are still "traveling around." An investigation of the mass-scale poisonings in Klimovskoye was initiated by the Cherepovets Rayon Public Prosecutor's Office on 27 January.

### Moscow Emergency Service Threatens Strike

927C0250D Moscow *TRUD* in Russian 12 Oct 91 p 2

[Article by I. Nevinnaya: "Emergency Service Is Ailing and Requests Help"; first paragraph is *TRUD* introduction]

[Text] Five ambulances, with flashing lights and sirens, stopped near the Mossovet building one day in October. For 10 minutes they were picketing there, after which representatives from the mayor's office and Mossovet were handed a letter-resolution of a meeting of representatives of substations of the Moscow First and Emergency Medical Aid Service.

The picketing was preceded by the following events. A group of physicians from the Central Substation gave warning to the chief physician of the Moscow Emergency Service, A. Shmatov, that an explosive situation had developed at the station staffed by 8000 people: They were dissatisfied because questions of fair wages are not being resolved and working conditions have not improved for many years; there is no social protection of medical workers.... As a result, many, very many do not simply resign, they run from the station. In the physicians' words, this conversation did not lead to anything, and then, three days later, a meeting of representatives of 44 substations and structural subsections of the service was convoked. It is they who declared that they no longer trust the service's management, created a strike committee and called for the city management to take action.

The main item in their package of demands is to fire management and hold elections for a chief physician on an alternative basis.

Then there was an extraordinary meeting of the trade-union committee, which recognized the complete legitimacy of all of the demands of the strike committee, with the exception of firing the chief physician. Incidentally, the trade-union committee did not support Shmatov either. He declared that he could not work in the face of such lack of confidence and submitted his voluntary resignation.

On the next day there was another meeting, this time of substation heads. Management representatives advised the chief physician not to be too hasty in resigning and declared the actions and the very organization of the strike committee to be illegal. Continuing to discuss his resignation, the chief physician nevertheless promised that those guilty of disrupting work discipline and organizers of the picket would be punished strictly. He gave orders to establish a commission to investigate this incident. Physicians who participated in the protest action and station dispatcher had to write explanatory notes. But now let us hear the opposing sides:

Chief physician A. Shmatov:

"The conflict lies essentially in the fact that the wages of medical personnel at our emergency aid station are not sufficient for a normal life. The situation worsened extremely this year. Personnel turnover has grown, especially among drivers. During the last few months there were days when about 100 ambulances failed to show up. We addressed Yu. Luzhkov with the request to find a way to raise wages, and since August our drivers began to receive approximately 1200 rubles.... But the wages of medical personnel remained unchanged. It is very difficult to resolve this problem, for there must be differentiation of wages, depending on the specialty, qualifications of a physician and feldsher, as well as consideration of tenure, etc. Time is required for this.

I support entirely and whole-heartedly the demands of the strike committee, with the exception of the first item, my resignation. At the present time, there is such confusion in the health care system that we simply have no place to address our problems.... Yet very much is being done: An automated control system is being developed at the station, as well as computerization, the concept of cardinal reorganization of the structure of the first and emergency medical aid service. We must learn to earn money ourselves, and if this reorganization is implemented there will be an opportunity to do this.

As for the right of my service to strike, I do not uphold it. Picketing is, in my opinion, simply a hooligan prank. This is not the way to solve serious problems."

M. Vartopetov, physician in an emergency aid brigade, member of strike committee:

"Concerning a strike by physicians and feldshers.... We do not tolerate a struggle in the form of refusal to respond to patient calls, and incidentally this is written in the resolution of the meeting. The problems we are discussing have plagued the service for many years

already, and this is felt first of all by patients. At present the situation is critical. Since the first of the year 24 physicians and 17 feldshers have resigned from my central substation, there being a total of 79. We are on the brink of dissolution of the service, it will simply cease to operate.

About the picketing. We used vehicles servicing expressly this rayon, the center of Moscow, for this purpose. The vehicles were in their own territory and were ready to respond to calls at any second. As a result, not a single patient was affected."

L. Kolosov, chairman of the Mossovet permanent commission for health care:

"All of the striker committee demands are justified and legitimate. In my opinion, A. Shmatov is mistaken in that, while he devotes much effort and time to future development of the service, he has ignored the interests of rank and file staff members for a long time. It would seem so simple to organize normal hot meals at the substation (after all, work goes on there around the clock) and to provide personnel with special uniforms.... The conflict would not have gone so far.

Today, however, one can apparently settle the situation only by holding alternative elections for a chief physician. Incidentally, there is nothing to prevent Anatoliy Shmatov, a highly qualified specialist, to declare his candidacy.

At present, our commission is familiarizing itself with the situation in the substations of the service. The results will be submitted to the Moscow administration. It is the one to make the final decision.

### **Food Products Spoil as High Prices Reduce Sales**

927C0353A Moscow KOMSOMOLSKAYA PRAVDA  
in Russian 20 Mar 92 p 1

[Article by O. Volkov]

[Text] In the words of the city's chief public health physician N. Shestopalov, the quantities of spoiled food are growing ever larger, even in the stores.

"What we predicted is happening," said Nikolay Vladimirovich. "The stores are unable to sell all of their products, primarily because the prices are a little too high. Each week we discover from one to two tons of 'outdated' products—fish, sausage, bakery goods."

The city's chief public health physician advises not buying any homemade preserved goods, milk, dairy products, cheese and meat in the streets.

### **Contaminated Food Imports Sequestered**

927C0353B Moscow KOMSOMOLSKAYA PRAVDA  
in Russian 20 Mar 92 p 1

[Article: "And This Time"]



[Text] A large consignment of grain was sequestered by the epidemiological station in Orenburg. It is believed that the grain, which was recently imported from Canada and Turkey, contains a pathogenic fungus.

### **Strike Committee Protests Closing of Armenian Oncology Center**

927C0258A Moscow TRUD in Russian 4 Dec 91 p 4

[Article by A. Ambartsumyan: "An Immense Problem"]

[Text] A strike committee was formed at the republic oncological dispensary situated in Yerevan. This was prompted by the decision of M. Nazaretyan, Armenian minister of health, to eliminate the republic oncological dispensary in the center of the capital of Armenia and to move the polyclinic operating there to outskirts of the city and place it under the jurisdiction of another oncological center located there.

In the opinion of the strike committee, as conveyed to the Snark information agency, it would be unwise, to say the least, to leave almost 1.5 million urban residents without a dispensary, the services of which are used by more than 100,000 people annually. The physicians add that it would also be immoral to send people requiring daily outpatient care to a region far from the center of Yerevan, which is difficult to reach, even for a healthy person, without his own car filled with commercial gasoline. They demand that the minister's order be rescinded.

Professor M. Ayrapetyan believes that "the minister's decision, if it is implemented would break down one of the most important structure of Armenian health care.

### **Kuzbas Medical Workers Strike**

927C0258B Moscow TRUD in Russian 11 Dec 91 p 1

[Article by Yu. Kotlyarov, Kemerovo: "Physicians Have Lost Their Patience....," first paragraph is TRUD introduction

[Text] Yesterday, the medical workers of Kuzbas [Kuznetsk coal basin] declared a three-day warning strike.

In spite of the "neutrality" of the region's administration, the presidium of the oblast council was able, although with great difficulty, to find the millions needed to start payment of compensation amounting to 150 percent of wages in accordance with the decision of a session of the oblast council of people's deputies. The funds for this purpose were transferred by many enterprises and even private individuals. An additional 300,000 hard currency was requested for the purchase of drugs and medical equipment. However, the Supreme Soviet and government of Russia, to whom the suggestions of the session of the oblast council and strike committee were forwarded in the nature of legislative initiative, remain silent. Yet, as before, there is nothing

to treat patients with in the hospitals, there is a shortage of products, bed linens.... The situation is growing increasingly critical. There have already been instances where desperate patients have beaten up medical personnel.

It is in such circumstances that the strike began, but nevertheless the first aid service responds to emergency calls and physicians do see patients in acute need of treatment at the polyclinics.

As reported in the oblast strike committee, as of 1400 hours local time, yesterday, 96 percent of the medical workers of Kuzbas as a whole and 76 percent of those at the oblast center participated in the strike.

### **Magnitogorsk Emergency Medical Service Personnel Threaten Strike**

927C0258C Moscow SOVETSKAYA ROSSIYA in Russian 30 Jan 92 p 1

[Article by TASS: "Demands by Medical Workers"]

[Text] There should be market wages for the market prices! This is one of the main demands of the staff of the city emergency service station who picketed the House of Soviets in Magnitogorsk.

The participants at the meeting declared that if their demands to strengthen social protection are not met they reserve the right to participate in the All-Russian strike of health care workers, which has been postponed to 26 February.

### **Venereal Disease Institute Lacks Basic Drugs**

927C0258D Moscow TRUD in Russian 4 Dec 91 p 4

[Article by A. Nikonov, under the rubric "Medicine and Life": "Lice, Scabies, What Next?"]

[Text] Do you know that herpes infections in the USSR are not very widespread in contrast to the West? The English are amazed: what a resistant people!

The Central Scientific Research Institute of Dermatology and Venereology is the only one in the nation that investigates diagnostics and methods of preventing dermatovenereological diseases.

In spite of the fact that the institute is situated in the nation of Soviets, things are not as bad there as they could have been, and although our professor "costs" one-seventh to one-tenth of what a western laboratory technician does and people are leaving for medical cooperatives, they still manage to develop some things at the institute. It has relatively modern equipment for laser therapy, electron microscopy, phototherapy, and biochemical tests. Some new diagnosticums and methods of treating pregnant women with syphilis have been developed....



However, it has already become difficult to replace imported ultraviolet lamps in therapeutic units. There is a shortage of simple vaseline, tar and iodine. There are no dermatological agents. There are no deliveries of the much needed naphthalan ointment, Azerbaijan under fire has other things to worry about. For the time being, there are enough drugs for treatment of both adults and children with venereal diseases. Yes, for children! Children contract them in nursery schools, they contract congenital syphilis, they become infected as a result of rape and everyday contacts.

The institute has only 80 beds per 1000 desiring treatment over the entire Union. All 30 sexually transmitted diseases are treated there. Many of them are virtually unnoticeable, but lead to sterility and impotence.

More recently, for reasons that are not entirely clear, itch has become very widespread and new forms of the disease have appeared that are not immediately identifiable even to dermatological specialists. The vectors of these forms are cats, rats and mice, particularly those bred in the old parts of the city, for example, Taganka. A new and effective ointment was developed for scabies but ... there are no raw materials to produce it.

Unfortunately, pesticides and, in general, all of our foodstuffs that are profusely "enriched" with chemicals contribute to the spread of dermatological diseases.

Apparently, pediculosis, i.e., louse infestation, has become widespread in recent times due to the "good" life. The uncontrolled migration of large numbers of homeless people, refugees, has played far from the smallest part in this.

"Well, what if we run out of drugs against louse infestation," I asked, "would you really wash patients' heads with kerosene, following the old-fashioned prescription?"

The medical workers responded firmly: "It means we will use kerosene."

Medicine is dying, but is not giving up! The only question is whether there will be enough kerosene.

#### **Private Development Fund for Pharmaceutical Industry Established**

927C0258E Moscow TRUD in Russian 4 Dec 91 p 4

[Article by A. Semenov: "This Is Our Last ... Fund"]

[Text] One cannot cover up this shame, as they say, with the hand: An extraordinary situation developed in the nation with respect to furnishing drugs to the public. Today the problem is perhaps as acute as the food problem. If the situation is not remedied, the breakdown that has developed in the medical industry will lead to a tragedy that will be considerably greater in scope than the one at Chernobyl.

The disintegrating government is no longer able to solve the medication problem by itself. What to do? Blue-collar workers, engineers and white-collar workers at enterprises, scientists at institutes and research centers involved in development and production of drugs and medical agents have decided to answer this question with specific action. They instituted the Fund for Development of the Medical Industry and have each deposited one day's wages in it.

A few words about the fund. This is a self-governed and developing extragovernmental organization that has set itself the task of financing a part of the special-purpose programs of accelerated development of enterprises and, on their basis, increased production of drugs and items to be used for medical purposes, development and introduction of new and highly effective domestic agents. Anyone from our country or abroad, any enterprise and organization can become a member of the fund. There are no limitations to depositors. But expenditures are made only for development of a modern, domestic pharmacological industry.

The fund's account number is 700715, TsOU [Central Administrative Department], USSR Gosbank [State Bank], MFO [Moscow Finance Department] 299112.

#### **'Soyuzfarmatsiya' Warns of Further Drug Price Increases**

927C0259A Moscow KOMSOMOLSKAYA PRAVDA in Russian 21 Jan 92 p 4

[Article by M. Guseva, "Prices for Medication: You Could Die"]

#### **[Text] Yesterday**

Retail prices for medicines in January quadrupled on average. However, wholesale prices still remained much higher. Deliveries of ready goods to pharmacies did not increase, and they continued to operate at a loss.

#### **Today**

All of our problems with lack of medicines have flowed smoothly across from the USSR to the CIS. Just as before, there is a shortage of raw material and packaging, things are not going well with import shipments.

At "Soyuzfarmatsiya" Association (which still exists, despite the elimination of Soviet agencies), we were told: "Agreements for 1991 between plants that make finished goods and raw material suppliers were concluded in September-October 1990; such agreements for 1992 have not been concluded as yet." When settling payment, almost no one is interested in money, only barter.

In such a situation, of course, we cannot count on seeing drug store shelves filled up very soon.

**Tomorrow**

Specialists at "Soyuzfarmatsiya" tell us that prices will climb even higher, but not for all medicines. A list of two hundred items has been drawn up in which nearly all groups of medicines are represented in one way or another.

The list includes widely used products: alcohol, aspirin, vapidol, korvapol, iodine, citramon, naphthizine, napa-zol, activated charcoal, nitroglycerin...

Their price is to be fixed, i.e. at today's already quadrupled price; a State subsidy will cover the difference between the wholesale and retail value.

Prices for other drugs are free floating. They are determined as the wholesale price plus commercial markup. Wholesale prices are not limited by anything. And markup, which is supposed to cover the work of the drug store itself, so far does not exceed 25 percent. In future, its level will be regulated by the State.

Not so long ago, a merchant could buy cotton wool from industry for something like eight rubles a kilogram, and sell it for about 75 rubles. Now, wholesalers want 100 rubles for a kilogram, and they will get it; the buyer will have to come up with a minimum of 125 rubles to acquire the same goods.

The "list of two hundred" does not include analgin, valocordin, bandages, mustard plasters, many kinds of cough drops. In other words, what matters most is not the physician's recommendations, but how fat is your purse. If you have money, then treat your headache with analgin, if not, then use citramon.

In addition, at the same time, measures of social welfare and categories of beneficiaries so far have not changed. Privileges are offered to children younger than three years, the chronically ill, veterans and invalids, refugees of Afghanistan and Chernobyl, badly-off pensioners...

Incidentally, some economists view the creation of a "special list" as a far from progressive measure. Medicines appearing on the list are at the same time among items of the greatest scarcity. They will immediately be bought up, and not just because they are relatively inexpensive. They will simply be taken at a disadvantage for sale to the drug stores themselves. The State subsidy for these would be paid to drug stores only after sale.

**Forecast**

No one has undertaken to state that our pharmaceuticals will be saved by rolled back prices. Not long ago, a 50-milliliter bottle of rather popular pantocrine cost about two rubles, the cost of a kilogram of the initial raw material being about 500 rubles. These figures have now risen to 90 and 6000 respectively; international buyers are offering the same amounts in SKV [not further identified]. You can guess for yourself where it is going to go first.

Nevertheless, there is still hope.

1. Free prices will appear not tomorrow, but as old stocks are sold and replaced with new goods bought by merchants from industrialists at wholesale prices that are already liberalized. So you might get lucky on your next trip to the drug store.

2. By presidential edict, more than 1 billion non-exchange rubles have been allocated for purchasing medicines, raw materials, instruments and equipment for Russia from abroad.

3. In spite of the confusion with contracts due to delays last year in import shipments, they are continuing to this day for 1991 accounts.

4. Talks are being held about developing new measures for social welfare, and the day may come, for example, when the doctor will hand to you with your prescription a social security coupon for which you will receive compensation for medicines purchased.

**Official Moscow Demographic Statistics**

927C0259B Moscow IZVESTIYA in Russian  
23 Jan 92 p 1

[Note, "Demographic Situation in Moscow Desperate"]

[Text] There were only 9.4 births per 1000 inhabitants in Moscow in 1991 as compared with 10.5 in 1990. The death rate has not changed, remaining 12.8 per 1000 as before. Such are the first estimated data of the Moscow Municipal Committee on Statistics.

**Moscow Enterprise Begins Production of Scarce Drugs**

927C0260A Moscow ROSSIYSKAYA GAZETA  
in Russian 12 Feb 92 p 1

[Article: "Bacteria Suffer a Defeat"]

[Text] Recently, the small enterprise KONPO, working at the Scientific Research Institute of Applied Microbiology in Podmoskovye mastered production of several scarce drugs.

"Our enterprise has produced the first batches of bifidumbacterin and cidepol," said V. Batargin, director of the enterprise, "the former drug is very effective in the treatment of acute intestinal infections—dysentery, salmonellosis, as well as combined therapy of sepsis, pneumonia and other suppurative infectious diseases, but the demand for it is met by no more than 30 percent. For this reason, when we brought a trial batch of this drug to one of the pharmacies in Moscow Oblast, it was sold out in an instant.

Cidepol is indicated for the prevention of venereal diseases. This development turned out to be so good that it has been patented by several pharmaceutical firms in the West.

**International Aid Representative Visits  
Yekaterinburg**

*927C0260B Moscow ROSSIYSKAYA GAZETA  
in Russian 12 Feb 92 p 1*

[Article: "Help is coming, but Problems Remain"]

[Text] "We do not need products at the present time," declared the director of one of the joint enterprises in Yekaterinburg to a representative of the International Institute for Humanitarian Aid, in answer to the latter's

attempt to determine why no powdered milk and butter have been exported by anyone from Stuttgart for a month. However, it is not only this answer of the businessman that caused the guest to become excited, writes the newspaper URALSKIY RABOCHIY. In the first place, in a week's stay in Yekaterinburg he was unable to determine what had happened to a previous shipment of clothing. In the second place, none of the local representatives of management received him, because they were all busy expressly with problems of ... supplying goods to the public.

# **UK, Polish Experts' Findings on Psychiatric Malpractice in Russian Children's Homes**

927C0265A Moscow KOMSOMOLSKAYA PRAVDA  
in Russian 1 Feb 92 p 5

[Article by Ya. Kozheurov and S. Mikhalych: "What Children and Dissidents Have in Common: Unknown Pages of Modern Psychiatry"]

[Text] *Eight years after we were excluded from the World Psychiatric Association for using psychiatry for political purposes, and two years after we were conditionally reinstated, a group of British experts, having completed an inspection tour in our nation at the invitation of people's deputies, has discovered something strange, literally: "some similarity between 'treatment' of political dissidents with enormous doses of drugs in the sixties and seventies, and use of the same medicines for 'treatment' of orphans in children's homes and psychiatric hospitals."*

The editorial staff has managed to obtain reports by the British group of experts headed by Baroness Cox, a member of the House of Lords and well known defender of civil rights, specialists of the Warsaw Office of the international organization "Physicians of the World," and the commission of the V. I. Lenin Children's Fund; we consider it necessary to publish some data from these reports.

## **Diagnosis Final and Not Subject to Appeal**

A psychiatric diagnosis, whether given at birth or thereafter, is final for practical purposes and is not reconsidered throughout life. Children are automatically sent to a children's home for the mentally retarded. Even though it is known that some diseases, such as delayed mental development, are subject to correction.

Early, postnatal diagnosis, which is widely practiced in our nation, generally gives a high percentage or erroneous diagnoses. In the West, for example, following a diagnosis of "encephalopathy," a child is observed for as long as 10 years, and if the symptoms of the disease are insignificant or totally absent, the diagnosis is cancelled. Here as a rule (especially if a child is an orphan or from a poor family), the first diagnosis is changed to "oligophrenia in a stage of moderate retardation," since living conditions in orphanages and children's homes are conducive to social degradation of the personality.

Only the patient's parents can submit a request for cancelling a diagnosis. In this context, no consideration is taken of the fact that a great many families would even be ready to make additional payments to keep up the "support" of their child.

Polish experts listed four reasons for misdiagnosis: absence of specialists (we do not train pediatric psychiatrists and psychologists), use of diagnostic norms that are overstated by comparison with international standards, internal instructions with requirements so overstated that most children fall into the category of moderate retardation and mental deficiency without any real

basis; particularly defenseless are children whose anamnesis "contains disadvantaged familial, social or prenatal circumstances, even if no clinical symptoms are observed," as well as children who have some inherent physical underdevelopment.

Diagnoses of "encephalopathy" and "oligophrenia" are made on scales that are cause for grave concern. The examination is often nominal, and takes a few minutes. In making the diagnosis, consideration is taken not so much of generally accepted tests and scales, as the inclination of the parents to drug abuse and alcoholism, their age, and social standing.

According to existing rules, only medical-pedagogical commissions can diagnose a child attending school and send that child to specialized institutions. In practice, this rule is constantly broken, and medical examinations are done at the request of teachers who have been annoyed by a child.

According to Polish data, of 48 children diagnosed as "moderately retarded" or "mentally deficient," 41 were normal, and the "stated disturbances were merely a consequence of living conditions in children's homes, boarding schools, or in the family."

According to British experts, from 36 to 70 percent of the examined children (depending on the diagnosis) are normal.

Upon individual examination, the number of children who could live normal lives without being isolated from society and with happy prospects for the future is considerably greater, roughly two-thirds.

## **Injections for Poor Progress...**

In almost all advanced nations, delayed mental development is regarded as a problem of education and is eliminated or alleviated by purely pedagogical methods. On the other hand, we consider it an incurable disease, and control it with drugs and strait jackets. The advisability of such treatment is dubious, even when it comes to deeply disturbed children, and what is to be said about those "erroneously" considered ill?

If a child with a level of development below average is provided with special conditions for development, he might "make up the slack" with the course of time. This is really impossible for us, because children suffering from mental retardation are kept isolated, without contact with "normal" children of the same age, and their education is limited to four grades.

Degradation is further aggravated by drug therapy. Drugs in pills and in the form of injections are constantly used, sometimes without a doctor's prescription. "Preventative" treatment is used, where the inmates of children's homes are administered large doses of magnesium sulfate once every 10-15 days in spring and autumn, and local anaesthesia is even used to reduce painful sensations.

Extensive use is made of psychotropic drugs such as amazin that is used throughout the world for treating schizophrenics. Injections may be given forcibly. Sulfozin, which was prohibited in 1990 (in the thirties in the West), is used in spite of injurious side effects: temperature as high as 40°C, high fever, rheumatic pain throughout the body. There have been cases of using neuroleptics, which are actively used in specialized psychiatric hospitals for convicted criminals.

Since medicinal drugs are used over a prolonged period in high doses, such "treatment" has a destructive effect on the nervous and endocrine systems, the liver...

Drugs are used as punishment for escape, poor progress, aggressiveness, and attempts to protest against the existing regime. Usually in such cases the child is sent to a psychiatric clinic for "examination." In some regions there are even standing orders from psychiatric hospitals for children's homes: a specified number of patients per month. "Especially distinguished" children are sent for a few months to clinics instead of to summer pioneer camps. Workers of the Children's Fund have established cases where the administration of the children's home subsequently declined to pick up their inmates from the clinics.

#### Deprivation of Civil Rights

Upon completion of instruction in the children's home, children with a fourth-grade education are sent by directive order to a place of employment. As a rule, these are factories where they perform monotonous, dirty, manual labor.

They live in factory dormitories where they are obliged to report before 10:00 pm, and have no right to have guests. The existing identity card and verification system does not permit them to leave independently; they will inevitably be caught and returned to clinics. They have no right to vote, are adjudged incompetent, have no opportunity to change their place of residence, employment, learn on their own, have no conditions for starting a family.

The British specialists justly note: The system is aimed at isolating all who are socially disadvantaged and at not dealing with their problems.

Moreover, KOMSOMOLSKAYA PRAVDA has exhibits showing that

—children are sent abroad for education to evade the endless queue in our nation;

—special "orphan" army formations were once set up that were used on "internal fronts";

—and there are other reasons that the All-Union Psychiatric Association was excluded from the World Body.

#### KOMSOMOLSKAYA PRAVDA Has Started an Investigation.

We are hoping for assistance from psychiatrists, teachers, and all who have additional information. Our telephone is 257-28-72.

### T- and B-System Immunity Status in Digestive Organ Disease Patients Exposed to Internal Radiation

927C0188B Kiev VRACHEBNOYE DELO in Russian No 11, Nov 91 (manuscript received 20 Jun 91) pp 17-20

[Article by N. G. Bychkova, V. G. Perederiy, and A. A. Fomina, Chair of Facultative Therapy, Kiev Medical Institute; UDC 612.017.1:616.3-085.849.5]

[Abstract] Systemic and local immunity were investigated in 534 people with ulcers, chronic gastritis, chronic gastroduodenitis, chronic cholecystitis, and chronic hepatitis, 282 of which were also involved in the clean up at Chernobyl. The observations began in April 1987. Erosive damage to the stomach and duodenal mucosa was found in 29.4 percent of digestive organ disease patients exposed to radiation (group I), while this figure was 12 percent for those digestive organ disease patients not exposed to radiation (group II). Group I also experienced more recurrences of ulcers after treatment than did group II. Investigation of cellular and humoral immunity revealed that the T-lymphocyte level during the exacerbation period was sharply depressed in all patients. Comparison of immunological indexes in duodenal and stomach ulcer patients did not reveal any differences in the levels of the main lymphocyte populations. The results demonstrated that imbalance among the immunoregulatory subpopulations of T-lymphocytes plays a significant role in the development of dysimmunoglobulinemia, which accompanies these diseases. In addition, investigation of immunocompetent cell levels in the stomach and duodenal mucosa biopsies indicated no correlation between the activity of the inflammatory process in the mucosa and its infiltration by lymphoid elements. In conclusion, these results suggest that there are pronounced changes in the immune system in digestive organ disease patients exposed to internal radiation that particularly affect the course of the disease. It is recommended that comprehensive treatment with immunocorrective agents be included in therapy for most digestive organ disease patients. References 6; Russian.

### Enhanced Radiation Resistance of Body Due to Transfusion of Autogenic Blood Irradiated With Low Doses of Ionizing Radiation

927C0188C Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 5, Sep-Oct 91 (manuscript received 10 Dec 90) pp 669-674

[Article by A. V. Kolodin and N. I. Arlashchenko, Scientific Research Test Center for Radiation Safety in Space Installations, USSR Ministry of Health, Moscow; UDC 577.391]

[Abstract] The efficacy of using an autotransfusion of blood irradiated with low doses of ionizing radiation to increase the body's total nonspecific resistance to radiation was investigated in 200 F<sub>1</sub> CBAXC57B1 mice. The

blood was drawn from the animals and irradiated with 0.05-0.5 Gy (0.3 Gy/min) of ionizing radiation and then returned to the mice by means of subcutaneous injection (0.1 cm<sup>3</sup> blood). The animals were then exposed to 9 Gy (0.3 Gy/min) of ionizing radiation one or 10 days later. The results demonstrated that those mice given a transfusion of irradiated blood had a much higher survival rate. A one-day interval between transfusion and total irradiation was shown to be more effective than a ten-day interval. In addition, although all doses of irradiating the blood were effective to some degree, 0.3 Gy was shown to be optimal. The beneficial effect of irradiating the blood, which is accompanied by erythrocyte hemolysis and direct radiation destruction of protein structures in the blood, is attributed to immunization of the body to radiotoxins. Accordingly, these results suggest that this method for enhancing the body's resistance to radiation by means of an autotransfusion of blood irradiated with low doses of ionizing radiation is effective. Figures 1; tables 1; references 10; Russian.

### Radionuclide Radiation Dosimeters

927C0188D Moscow MEDITSINSKAYA TEKHNIKA in Russian No 4, Jul-Aug 91 (manuscript received 20 Jun 90) pp 38-40

[Article by I. O. Vasilyev and Yu. N. Tarasenko; UDC 615.47.03:615.849.2.015.3.07]

[Abstract] The article discusses the various types of radiation dosimeters currently in use. There is a wide array of ionizing radiation dosimeters available to satisfy every user's need. However, people and objects are often exposed to more than one type of radiation. The existing dosimeters were built to measure only one type of radiation, and attempts to measure additional radiation levels skew the results. Accordingly, the authors recommend that existing dosimeters be modernized and new ones developed to measure mixed radiation. Tables 3; references 3; Russian.

### Antioxidant System Status and Cellular Proliferation Marker Level in Persons From Chernobyl Accident Zone

927C0191B Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 8, Aug 91 (manuscript received 02 Jan 91) pp 6-11

[Article by N. A. Grigorovich; UDC 616-001.28:615.035]

[Abstract] This article describes a clinical laboratory computer system for preclinical diagnosis of malignant tumors. It was used to investigate the antioxidant system status and cellular proliferation marker system in the victims of Chernobyl and a control group. One of the distinguishing aspects of this methodical approach is the use of mathematical methods to recognize patterns for classifying the subjects screened. The technique involves screening blood samples to separate people into three



groups: blood that is similar 1. to that from healthy people; 2. to that from people with oncological diseases; and 3. to neither that from healthy people nor oncology patients. The results demonstrated that the system had a sensitivity index of 79 percent and a specificity index of 90 percent. It was also shown that 12 months after the accident there were fewer persons in the experimental cohort with antioxidant system insufficiency than there were among the control group, with the exception of those who had received 5 REM (roentgen equivalent man) or more. In addition, 70-90 percent of persons who considered themselves to be essentially healthy but who had homeostasis disturbances typical of malignant tumor patients were shown to have pre-tumor diseases. Such instances were much more frequent among persons living in contaminated areas or having received 5 REM or more. Furthermore, the number of people with elevated biomarker levels and with a heightened risk of developing oncopathology increases with time. In conclusion, the use of these informative instrumental diagnostic methods should make it possible to reveal a given pathology when a patient can still be cured. Figures 3; references 35: 29 Russian, 6 Western.

#### Radioactive Cesium

927C0191D Minsk ZDRAVOOKHRANENIYE  
BELORUSSII in Russian No 8, Aug 91 (manuscript  
received 01 Feb 91) pp 47-50

[Article by I. I. Goncharik, Belorussian Scientific  
Research Institute of Radiation Medicine; UDC 546.36]

[Abstract] Of the 35 cesium isotopes, only  $^{133}\text{Cs}$  is stable. Isotopes  $^{134}\text{Cs}$  and  $^{137}\text{Cs}$  are of the most concern due to their long half-lives. After an accident, cesium settles on plants and in the soil to a depth of 3 cm. It dissolves well in water. Cesium enters animals primarily through their feed. Lactating animals eliminate some of the substance with their milk. Dairy and meat products are the primary means by which cesium enters the human body, followed by grains and produce. Nuclides entering with food are almost completely absorbed by the body. The half-life for eliminating cesium from the body ranges from 50 to 200 or more days. Increasing the intake of plant fiber significantly decreases the uptake of cesium. In addition, increasing potassium and sodium consumption accelerates elimination of the radionuclide by 38 and 31 percent, respectively. Analysis of his own results of examining 5,000 persons residing in the stringent control zone led the author to believe that hundreds of them, especially forest rangers, hunters, and fishermen, have incorporated high levels of radioactive cesium. The upper limits of normal for radioactive cesium incorporation are 0.1  $\mu\text{Ci}$  for children and 0.3  $\mu\text{Ci}$  for adults. Urgent measures for reducing the radionuclide level in the body include washing the face and hands with soap and water and the mouth with water or a salt solution. A daily dose of two to three g of ferrocene is recommended as well to help reduce the cesium level. In addition, persons with high cesium levels should enjoy a well-balanced diet. The author also cautions against the widespread erroneous

concept that alcohol has any significant radioprotective properties. References 12: Russian.

#### The Biological Effect of Ionizing Radiation in Low Doses (Review of the Literature)

927C0345A Minsk VESTSI AKADEMII NAVUK  
BSSR. SERYYA BIYALAHICHNYKH NAVUK,  
in Russian No 4, Jul-Aug 91 pp 110-114; UDC  
616-001-085.37:615.371/372

[Article by V. G. Vladimirov, S. P. Deyev, and N. V. Serkov; Institute of Radiobiology of the Belorussian SSR Academy of Sciences]

[Text] The last decade has been characterized by the expansion of the circle of persons who have various contacts with sources of ionizing radiation in the course of their occupational activity. At the present time they number from 3.8-4.6 percent of the total population in the developed countries. For comparison let us point out the fact that this number did not exceed 2 percent according to the data of 1972. A doubling of the number of those working with such sources is expected by the end of the present century. The problem has taken on special urgency after the tragic events of the Chernobyl NPS [Nuclear Power Station]. All of this in fact determines the interest in the problem of low doses of ionizing radiation.

The study of the biological effect of low doses of ionizing radiation is one of the most complex and the least investigated divisions of radiation medicine. Studies devoted to this question which have appeared have not clarified the situation. It is evident by now that in-depth, programmatic investigations are needed. However, before they are placed on the agenda, it is necessary to analyze all the available studies devoted to the biological effect of low doses of ionizing radiations.

In moving to the direct presentation of published data, let us define what we will include in the concept of "low doses". On this score there are in publications the most diverse points of view. Various authors regard doses to be low which differ from one another by factors of tenths and sometimes even hundredths<sup>1-3</sup>. In the opinion of A. M. Kuzin, doses less than 0.1 Gy should be considered low, i.e., doses for which a stimulating effect of irradiation on some biological processes is characteristic. A number of authors<sup>2, 4-6</sup> understand the minimally effective dose in relation to any biological phenomenon to be low.

Specialists working in the field of radiation hygiene, believe that a range of doses, starting with natural background levels and ending with maximally allowable levels, should be included in the ranks of low doses. In the presence of exposure to such doses no disturbances at all of the state of health of man should be expected<sup>7</sup>. However, it seems to us that 0.5 Gy should be accepted as the upper limit of low doses. Irradiation in doses exceeding this level, even if it does not induce the development of acute radiation illness, still may be the

cause of the so-called "reaction to irradiation" or "radiation reaction"<sup>8, 9</sup>. In other words, in these cases it has been possible to record clinically an acute radiation injury already.

Most of the information on the biological effect of low doses has been obtained in animal experiments. It has been demonstrated, in particular, that irradiation in doses from 0.01 even up to 0.05 Gy can lead to some increase in the blood leukocyte content which does not exceed the limits of physiological fluctuations<sup>10</sup>. The exceeding of the upper boundary of this dose limit was the cause of the development of a slight leukopenia (the number of leukocytes decreased by 20-30 percent). A decrease took place in the number of stem cells and myelokaryocytes, the number of aberrant mitoses increased, and the number of lymphocytes in the peripheral blood decreased<sup>11-14</sup> at the same time. It should be noted, however, that these changes, with the exception of the chromosomal aberrations, were unstable, and usually disappeared practically completely by the 20th-30th days after the exposure to the ionizing radiations. Nevertheless, it would be premature to view these data as proof of the complete normalization of hematopoiesis overall.

An increase in the number of chromosomal aberrations in irradiated cells is one of the important indicators suggesting a substantial influence of low doses on the organism<sup>2, 15</sup>. Disruption of the structure of genetic material in the presence of irradiation has been observed in various human cells and experimental animals<sup>15-18</sup>. It has been established that the number of types of chromosomal aberrations increases in direct proportion to the dose and exposure rate. The investigation of the cytogenetic disturbances in peripheral blood lymphocytes is widely used as a unique dosimeter, starting with exposure at a dose of 0.05 Gy<sup>12, 13</sup>, and according to the data of A. V. Sevankayev<sup>16</sup>, this limit can even be substantially lower (to 0.01 Gy).

Data are available according to which the frequency of chromosomal aberrations increases substantially in the bone marrow over the course of nine to 27 months four to six years after daily irradiation at a dose of 1-1.5 rad<sup>18, 27</sup>. It has been shown in some studies<sup>19, 20</sup> that even the dose of X-rays received by a patient during diagnostic procedures is capable of inducing an increase in the number of chromosomal aberrations in blood lymphocytes. External therapeutic irradiation of the organism induces an even more pronounced mutagenic effect. It has been possible even three to 24 months after radiation therapy to discover an increased number of chromosomal aberrations in the peripheral blood of such patients.

It follows from the data cited that diagnostic, and all the more so occupational, irradiation with low doses of ionizing radiation, not to mention therapeutic exposure, induces the appearance of both stable and unstable aberrations in cells. The cytogenetic injuries are maintained

for a very long period, and may be the cause of the occurrence of remote post-radiational complications<sup>21, 22</sup>.

Chromosomal aberrations are by no means the only undesirable consequences of irradiation, and this is attested to by published data, especially those concerning the influence of low doses of ionizing radiation on the state of immunity<sup>23-26</sup>. The important role of the immune system in the maintenance of the internal milieu of the organism, as in the formation of a number of pathological states, is beyond doubt; this makes it possible to regard immunological shifts as a criterion of unfavorable influences of ionizing radiation. However, it is extremely difficult to state at the present time concretely what the consequences will be. It can only be asserted that the resistance of the organism to the influence of factors which are unfavorable for health will be diminished, and that the probability of the occurrence of various infectious diseases will increase<sup>35, 36</sup>.

The data available in the literature on shifts in the immune system following exposure to low doses of radiation are very disparate. If some authors<sup>25, 26</sup> assert that immunodepression arises following irradiation in a dose not less than 1 Gy, according to other data<sup>23, 24</sup>, a change can be found in the majority of immunological indices even after exposure to doses of 0.15-0.25 Gy.

It has been shown in a number of investigations carried out on humans that some decrease in the number of T-lymphocytes, the suppression of phagocytic activity of neutrophils, as well as the formation of autoantibodies can be found with irradiation even at doses which do not reach the maximal allowable doses for professionals<sup>23, 24, 36</sup>. The temporary depressive effect of ionizing radiations is not limited to the T- and B-lymphocytes, but extends to the monocytes and the stem cells. Immunocompetent cells are capable of keeping and accumulating genetic disruptions, and this can finally lead to the development of functional defectiveness of these cells and of the immune system as a whole<sup>29</sup>.

A change in the properties of the so-called adherent cells and a quite profound suppression of thymus-dependent antibody-formation have been found in experiments on mice<sup>31</sup>. By contrast with humans, the restoration of the T- and B-lymphocyte count took place in mice quite rapidly after irradiation. The post-radiation immunodepression that was maintained could have been determined by the functional defectiveness of the lymphocytes, by the activation of suppressor cells, or by the inadequacy of the microcirculation<sup>32, 37</sup>. To an even greater degree than the disruption of the functioning of individual cellular elements of the immune system, irradiation suppresses the capacity of the cells for cooperative interaction. For example, a stable suppression of the primary and secondary migration of T-lymphocytes into the lymph nodes was identified in the case of sublethal (including following exposure to a dose of 1 Gy) irradiation of mice; this, as has been conjectured,

suggests damage to the receptors of the lymph nodes. This activity remained at a low level as far as the third month following irradiation, and recovered only to 50 percent after a half year<sup>30, 31</sup>. The ultrastructural disturbances of splenic lymphocytes were studied by electron microscopy. It was possible to establish that changes in the structures of the nucleus and some components of the cytoplasm of the cells, as well as a pronounced functional polymorphism of the mitochondria, occur four hours and three days after irradiation at a dose of 0.5 Gy. A change in the electron density of the mitochondria took place simultaneously; this change was interpreted by the authors as evidence of their functional stress and of the manifestation of post-radiation dystrophy<sup>37</sup>.

Experimental data have been obtained regarding the disturbance of the functional properties of the surface membranes of erythrocytes occurring upon exposure to low doses of ionizing radiation<sup>28</sup>. As early as three hours after irradiation of rats at doses up to 1 Gy, a decrease has been observed in the level of the membrane potential of erythrocytes. A significant increase in the flux of potassium out of erythrocytes from the first through the seventh day has also been identified. All of this is regarded as evidence of the fact that changes take place in the functional properties of the surface biomembranes of erythrocytes in the initial period following irradiation with low doses.

At the present time data are available relating to the fact the endocrine system is one of the loci which are vulnerable in the presence of irradiation, including exposure to low doses of radiation. It has been shown in a number of studies<sup>32</sup> that the reception of a number of steroid hormones (androgens, progestins, estrogens, and glucocorticoids) is disturbed as early as 24 hours following irradiation at doses of 0.5 and 1 Gy. This effect is dose-dependent and is maintained for a long (up to six months) time after irradiation.

Information is also available regarding a disturbance in energy exchange and in the microstructures of the cells of the endocrine glands, the myocardium, and the liver of rats irradiated with low doses. A decrease in the activity of the aerobic mechanisms of energy generation took place in the cells of the thymus as early as the first day after irradiation with a dose of 0.5 Gy. A similar pattern has also been observed in the acini of the pancreas. Here, at the same time, structural changes were also identified at later periods: the overgrowth of connective tissue took place, and lymphocytic infiltration and phenomena of the stagnation of blood in the vessels developed as well. Substantial changes were found in the myocardium, liver, and adrenals of the irradiated animals. Thus, small focal necrotic changes have been identified, an increase in the permeability of membranes took place, and ultrastructural alterations have been discovered in the chromatin of mitochondria as early as the end of a month following exposure to a dose of 1 Gy<sup>33</sup>.

No less interesting are data concerning substantial changes in the mediator interrelationships in brain structures<sup>34</sup>. Suppression of a number of neuromediator processes are observed as early as two hours after irradiation with a dose of 0.5 Gy; the most substantial level of these disturbances was reached by the sixth month. This reveals the causes of a number of vegetative disturbances which are characteristic for exposure to low doses of ionizing radiation.

All the foregoing suggests that exposure to low doses of ionizing radiation induces multilevel changes in different organs and systems. However, despite the available data, it can be concluded that the majority of these questions remain poorly studied at the present time. Many authors have assessed the effects of low doses of ionizing radiation on the basis of individual parameters which characterize changes in one system or another, but which do not make it possible to form notions of the disturbances taking place in the organism as a whole. At the same time, judging from an analysis of published data<sup>35, 36</sup>, disturbances in the immune system are observed in the presence of prolonged irradiation with low doses, as the result of which the defensive forces of the organism are reduced, and conditions are created for the activation of latent infections. And although convincing evidence is lacking at the present time of substantial harm to human health which might be caused by irradiation at doses lower than 0.5 Gy, the above conclusion still does not imply that the problem of the biological effect of low doses of radiation can be taken off the agenda.

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# **Production of Standard Anthrax Bacteria Antigen From Vaccine *Bac. anthracis* Strains**

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No 7, Jul 91 pp 30-31

[Article by A. A. Manichev and B. I. Shmorgun, All-Union State Control Scientific Research Institute of Veterinary Preparations; UDC 619:576.809.7]

[Text] One of the principal methods of diagnosing anthrax is the Ascoli precipitation reaction. It is used to identify isolated microbial cultures and to study pathological material from dead animals, especially in cases where it is impossible to reveal anthrax agent bacteriologically due to lysis of the microbes. The precipitation reaction is used mandatorily when testing raw leather supplied by the population and imported from other countries for anthrax.

This reaction requires standard bacterial anthrax antigen, which is prepared by biological enterprises out of a vegetative culture of virulent anthrax strain ZBK<sub>2</sub>.

There is great scientific and practical interest in obtaining standard precipitating antigen from unencapsulated vaccine anthrax strain. This would permit exclusion of the possibility of infecting production workers with anthrax, infesting the environment with the agent of this disease, and contaminating the biological preparations made by the enterprise with virulent anthrax culture.

In order to reach this objective we studied the composition of heat-stable and precipitating antigens for nine vaccine and 24 virulent *Bac. anthracis* strains in a cross diffusional precipitation reaction. Disintegrates of 16-18 hour cultures of *Bac. anthracis* strains obtained by Grasse's method, as modified by A. A. Manichev (1984), by means of multiple freezing, thawing and autoclaving at 120°C for one hour, served as the antigens in the diffusional precipitation reaction. Single-strain sera were obtained by hyperimmunization of rabbits with the disintegrates.

All of the studied *Bac. anthracis* strains possessed one heat-stable precipitating antigen similar to the commercially available one. Thus the question as to the fundamental possibility of making a standard precipitating antigen out of any anthrax strain was answered.

The next stage of the work involved selecting a vaccine unencapsulated *Bac. anthracis* strain producing the given antigen in the largest quantity. For this purpose we tested the strains STI-1, Sh-15, 34F<sub>2</sub>, 55, 94 and 916-1.

In accordance with instructions currently in effect, we prepared standard precipitating antigens out of cultures of the indicated strains and tested them in the precipitation reaction using commercially obtained precipitating anthrax sera (there were a total of 93 series of sera). Commercial precipitating antigen was used as the control.

The data were subjected to statistical treatment using a programmable microcalculator and a computer program written by Yu. K. Bayun (1989).

It is evident from Table 1 that antigens obtained from strains 55 and 34F<sub>2</sub> possessed the greatest precipitating activity ( $P < 0.05$ ).

**Table 1. Activity of Standard Precipitating Antigens**

Bac. anthracis Strain	Antigen Activity (Time of Reaction's Onset, sec)
55	35.3 +/- 1.4
94	45.5 +/- 0.75
916-1	46.0 +/- 0.69
Sh-15	46.1 +/- 0.75
34F <sub>2</sub>	40.4 +/- 0.72
STI-1	42.4 +/- 0.65
M-71 (encapsulated strain—control)	46.1 +/- 0.92
3BK <sub>2</sub> (commercial antigen—control)	40.3 +/- 0.86

**Table 2. Activity and Specificity of Test and Control Samples of Standard Bacterial Anthrax Antigen**

Standard Bacterial Anthrax Antigen, Series Number	Time of Precipitation Ring Formation (sec) With											
	Archival Samples of Anthrax Precipitating Serum, Series Number										Normal Equine Serum	Physiological Solution
	50	51	52	53	54	55	56	57	58	59		
66 (commercial)	20	20	15	25	15	25	20	20	20	15	—	—
67 “	20	15	15	20	15	25	15	20	25	20	—	—
68 ”	20	20	20	20	15	20	15	15	20	15	—	—
69 “	25	15	15	20	15	20	15	15	20	20	—	—
70 ”	20	15	20	20	20	20	15	20	20	20	—	—
From strain 55	20	15	15	20	15	20	15	20	20	15	—	—
From strain 34F <sub>2</sub>	20	20	15	20	15	20	15	15	20	15	—	—

Experimental industrial series of standard bacterial anthrax antigen from strains 55 and 34F<sub>2</sub> produced by the Tobolsk Biological Factory were commission-tested (Table 2).

#### Conclusion

The commission believes from its tests that standard bacterial anthrax antigens from strains 55 and 34F<sub>2</sub>

are highly active and specific. They are not inferior in terms of this indicator to commercially obtained antigen from the virulent anthrax strain ZBK<sub>2</sub>.

Production of standard bacterial anthrax antigen from strains 55 and 34F<sub>2</sub> was introduced at the Tobolsk Biological Factory.

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### Ultrastructural Differences in Mitochondria of Two Types of Triticale Calluses

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[Article by S. N. Matveyenko, V. V. Ruban, L. N. Kaminskaya and L. V. Khotyleva, academician, Belorussian SSR Acad. Sci., Institute of Genetics and Cytology, Belorussian SSR Academy of Sciences; UDC [633.11+633.14]+576.311.347.085.23]

[Abstract] A comparative ultrastructural analysis was conducted on embryogenic and nonembryogenic calluses derived from germ buds of triticale GL-17 and T-441 grown on medium P8. Evaluation of 15 morphometric parameters revealed significant differences in certain parameters between the embryogenic and nonembryogenic calluses. The major difference was that mitochondria of embryogenic calluses were characterized by better membranous development which correlated with superior energy generation and, consequently, more efficient differentiation. Figures 2; tables 1; references 14: 4 Russian, 10 Western.

### Description of UkSSR Academy of Sciences Institute of Cellular Biology and Genetic Engineering

927C0308A Kiev BIOPOLIMERY I KLETKA in Russian Vol 7 No 4, Jul-Aug 91 pp 5-6

[Article by Yu. Yu. Gleba, director of the Institute of Cellular Biology and Genetic Engineering, Ukrainian Academy of Sciences, academician of the Ukrainian Academy of Sciences, member of the European Academy: "Cellular Biology"]

[Text] This issue of the journal consists of scientific articles by the scientists of the Ukrainian Academy of Sciences Institute of Cellular Biology and Genetic Engineering, which is the youngest biological institute in our republic. This institution was founded by the Ukrainian government last year, although it has been in existence as an independent department of the Institute of Botany since 1988. The foundation of the present institute consists of teams headed by Prof V. P. Bannikova, D. M. Grodzinskiy, academician of the Ukrainian Academy of Sciences, A. A. Sozinov, academician of the UkSSR Academy of Sciences and VASKhNIL [All-Union Academy of Agriculture imeni I. Lenin], and my department. At the present time we have a staff of 155 people 75 of whom are scientific associates (including 10 doctors and 50 candidates of sciences). The average age of the scientific associates is 37 years.

I believe that there is no particular need to introduce our scientific staff to fellow biologists. The institute already occupies a worthy place among related institutions in number of publications, including some in international periodicals, as well as frequency of citation and number of monographs published in the USSR and abroad. The

curriculum vitae of our scientists includes the following: USSR State Prize, UkSSR State Prize, International prize "For Contribution to Development of European Science" (Germany), Research Prize of the A. von Humboldt Fund (Germany), one recorded discovery, eight patents, etc. The institute is the chief organization of the Ukrainian Agricultural Biotechnological Center; it has been recognized by UNESCO as a "center of excellence," and in this capacity has already offered three international classes on plant biotechnology. The institute, along with the Kiev State University, has opened a department of cellular biology and engineering within the biology department, and is training specialized personnel for it. The main scientific directions of the institute are:

- 1) Analysis of organization and expression of genetic material in plant cells; 2) development of technology of somatic hybridization of the most important agricultural plants (*Solanaceae*, *Cruciferae*, *Leguminosae* and *Gramineae* families); 3) recovery of new original breeding material with use of cellular technologies, cellular and genetic engineering; 4) development of new methods of controlled transfer of genetic material among representatives of various plant species; 5) use of recombinant DNA technology to recover plant breeding material; 6) development of theory of reliability of biological systems; 7) investigation of radiobiological and radioecological sequelae of the accident at the Chernobyl Nuclear Power Plant.

The institute's plans for the immediate future include organization of combined biotechnological industries.

It must be stressed that the scientific output of the institute presented [here] to our colleagues for their evaluation is not the quintessence of what we are doing and is by no means an attempt to flaunt our accomplishments. In response to the request of the editorial board, we have submitted the results of research completed to date, which may be of interest to the readers of the periodical BIOPOLIMERY I KLETKA [Biopolymers and the Cell] and offer a time frame to our endeavors. For this reason, I should like to talk about the current state of affairs at the institute and our plans, since they have been insufficiently covered in other publications. We believe that we obviously do not have enough molecular-biological and genetic-engineering approaches. In this regard, more than one-third of our scientists have now left for long-term scientific training in the best foreign laboratories, and we hope this will result in their returning to us as better qualified specialists and setting up normal, sound ties with foreign research centers.

In addition to human parameters, there is also change in financial parameters that determine our scientific policies. For several years we have not been receiving any hard currency from the government for the purchase of instruments and reagents, and we received none this year even to acquire scientific periodicals. Under such conditions, the institute is compelled to

expend more and more of its energy on work that is financed by other countries. At the present time, we have research grants from American Cyanamid (Princeton, USA), Nunkhems (Holland), as well as from the Kerber Fund (FRG), UNESCO, the Federal Ministry of Research and Technology (FRG), and negotiations are in progress concerning joint work with Kelgin (Davis, USA), P.G.S. [Plant Genetic Systems] (Belgium) and others. I am writing about this without any

particular pride or joy. In the first place, it is very difficult to obtain these funds and, in the second place, the one who pays, calls the shots, as they say. I am already anticipating that the patriotism of our behavior in this respect will be questioned. It is quite patriotic, because it permits preservation of the qualifications of our scientists until a time, God willing, when our government will again have funds for "luxuries" such as basic science.

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